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Santa Barbara

Total Synthesis of Bioactive Marine Natural Products Inspired by Enolate Chemistry

&

Developments of New Haloalkylations via Soft Enolizations

A Dissertation submitted in partial satisfaction of the requirements for
the degree Doctor of Philosophy in Chemistry

by

Aaron Thomas Herrmann

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March 2015

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March 2015

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Developments of New Haloalkylations via Soft Enolizations

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by

Aaron Thomas Herrmann

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2. Gu, Z.; Herrmann, A. T.; Stivala, C. E.; Zakarian, A. "Stereoselective Construction of Adjacent Quaternary Chiral Centers by the Ireland–Claisen Rearrangement: Stereoselection with Esters of Cyclic Alcohols" *Synlett* **2010**, *11*, 1717-1722
3. Gu, Z.; Herrmann, A. T.; Zakarian, A. "Dual Ti-Ru Catalysis in the Direct Radical Haloalkylation of *N*-Acylloxazolidinones" *Angew Chem Int. Ed.* **2011**, *50*, 7136-7139

4. Herrmann, A. T.; Martinez, S. R.; Zakarian, A. "A Protecting-Group-Free Total Synthesis of Brevisamide: thru an Asymmetric Henry/Achmatowicz Rearrangement" *Org. Lett.* **2011**, *13*, 3636-3639
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6. Herrmann, A. T.; Alvarado, J.; Zakarian, A. "Stereoselective α -Fluorination of *N*-Acyloxazolidinones Room Temperature within 1 h." *J. Org. Chem.* **2014**, *79*, 6206-6220.

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ABSTRACT

Total Synthesis of Bioactive Marine Natural Products
&
Developments of New Haloalkylations via Soft Enolizations

by

Aaron Thomas Herrmann

Marine natural products have long served as promising compounds and scaffolds for new therapeutic agents; however, their utilization is often extremely limited due to poor availability from natural sources and their molecular complexity. Hence, synthetic investigation of utilizing innovative techniques offers shortcuts in the production of such agents and modification. Studies directed toward the synthesis of marine natural products and their scaffolds inspire the development of new, efficient, and economical methods that are useful for medicinal research and for the synthesis of new pharmaceuticals and organic compounds.

The first part of this dissertation focuses on the synthetic studies directed toward the synthesis of nuphar thiaspirane alkaloids. The main drive of this effort is to allow access to each of the four classes of nuphar thiaspirane alkaloids. During these studies, a new procedure for the generation of tetrasubstituted tetrahydrothiophenes

was developed. This method has been further applied for a late-stage Stevens rearrangement to generate each class of nuphar thiaspirane alkaloids from common intermediates.

The second part describes the total synthesis of the marine natural product (+)-brevisamide. The art and science of natural product total synthesis has become increasingly more associated with the various principles of the “economies” of synthesis. Evaluation of protecting group use serves as one metric of synthetic efficiency and can provide a framework for developing a synthesis plan. A new protecting-group-free synthesis of, the marine cyclic ether alkaloid, brevisamide was completed.

The third part describes the development of new and exciting chemical transformations revolving around haloalkylations of *N*-acyl oxazolidinones via Group IVa metal enolates by both radical and electrophilic methods. These studies include: mechanistic elucidation of trichloromethylations, perfluoroalkylation and trifluoromethylation methodology development, and a generic α -fluorination method.

The final part describes a new procedure for the generation of *syn*-1,3-diols, which addresses both stereo- and regiocontrol in the rhenium catalyzed transposition of allylic alcohols.

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List of Abbreviations

Abbreviation, symbol, or chemical formula	Term
9-BBN	9-borabicyclo[3.3.1]nonane
$[\alpha]$	specific rotation
α	alpha
AcOH	acetic acid
aq.	Aqueous
AgBF ₄	silver tetrafluoroborate
AgClO ₄	silver perchlorate
AgOTf	silver triflate
AuCl ₃	gold(III) chloride
β	beta
BF ₃ Et ₂ O	boron trifluoride diethyl etherate
Bn	benzyl
BnBr	benzyl bromide
Boc	<i>tert</i> -butyl carbonate
Boc ₂ O	di- <i>tert</i> -butyl dicarbonate
br	broad
brsm	based on recovery of starting material
BrCCl ₃	bromotrichloromethane
BSA	bis(trimethylsilyl)acetamide
Bu	butyl

Bu ₄ NI	tetrabutylammonium iodide
Bz	benzoate
BzCl	benzoyl chloride
°C	degrees Celsius
c	concentration
¹³ C	carbon 13
calcd	calculated
CBz	benzyloxycarbonyl
CCl ₄	carbon tetrachloride
CDCl ₃	deuteriochloroform
C ₆ D ₆	deuterobenzene
CD ₃ OD	deuteromethanol
CF ₃ CO ₂ CH ₂ CF ₃	2,2,2-trifluoroethyl trifluoroacetate
(CF ₃ CO) ₂ O	Trifluoroacetic anhydride
CH ₂ Cl ₂	dichloromethane
CH ₂ O	formaldehyde
CH ₃ CN	acetonitrile
C ₂ H ₄ Cl ₂	1,2-dichloroethane
(COCl) ₂	oxalyl chloride
CrO ₃	chromium(III) oxide
CSA	camphorsulfonic acid
Cs ₂ CO ₃	cesium carbonate

CuBr	copper(I) bromide
CuBr·Me ₂ S	copper(I) bromide dimethyl sulfide complex
CuCl	copper(I) chloride
Cu(OAc) ₂	copper(II) acetate
δ	chemical shift(s)
d (NMR)	doublet
d (time)	days
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DDQ	2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone
DHP	dihydropyran
DIPEA	di- <i>iso</i> -propylethylamine
DIBAL	diisobutylaluminum hydride
DMAP	<i>N,N</i> -4-dimethylaminopyridine
DMF	dimethylformamide
DMP	Dess-Martin periodinane
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO	Dimethyl sulfoxide
DPPA	diphenyl phosphoryl azide
DPEphos	(Oxydi-2,1-phenylene)bis(diphenylphosphine)
dr	diastereoseomeric ratio
DTMP	2,6-di- <i>tert</i> -butyl-4-methylpyridine

<i>E</i>	entgegen
EDCI	1-ethyl-3-(3-dimethylaminopropyl)-carbodiimidehydrochloride
<i>ee</i>	enantiomeric excess
EI	electron impact
equiv.	equivalent
ESI	electrospray ionization
Et	ethyl
Et ₃ N	triethylamine
Et ₂ O	diethyl ether
EtOAc	ethyl acetate
EtOH	ethanol
Et ₃ SiH	triethylsilane
Et ₃ SiOTf	trimethylsilyl trifluoromethanesulfonate
Et ₂ Zn	diethyl zinc
FeCl ₃ ·6H ₂ O	iron(III) chloride hexahydrate
g	gram(s)
GII	Grubbs Catalyst 2 nd generation
h	hour(s)
¹ H	proton
HCl	hydrochloric acid
HF	hydrofluoric acid
HfCl ₄	hafnium tetrachloride

HFIP	1,1,1,3,3,3-hexafluoroisopropanol
HGII	Hoveyda–Grubbs Catalyst 2 nd generation
HMPA	hexamethylphosphoramide
H ₂ O	water
HOBt	<i>N</i> -hydroxybenzotriazole
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
H ₂ SO ₄	sulfuric acid
Hünig's base	<i>N,N</i> -diisopropylethylamine
hν	light
Hz	hertz
ImH	imidazole
<i>i</i>	iso
I ₂	iodine
<i>i</i> -Bu ₂ AlH	diisobutylaluminum hydride
^{<i>i</i>} Pr ₂ NH	di- <i>iso</i> -propylamine
^{<i>i</i>} Pr ₂ NEt	di- <i>iso</i> -propylethylamine (Hünig's Base)
^{<i>i</i>} PrOH	isopropanol or (2-propanol)
IR	Infrared Spectroscopy
[Ir(COD)Cl] ₂	chloro(1,5-cyclooctadiene)iridium(I) dimer
KCN	potassium cyanide
KHMDS	potassium hexamethyldisilazane

K_2CO_3	potassium carbonate
KOH	potassium hydroxide
J	coupling constant
L	liter(s)
LDA	lithium diisopropylamide
$LiAlH_4$	lithium aluminum hydride
LiBr	lithium bromide
$LiBF_4$	lithium tetrafluoroborate
LiCl	lithium chloride
LiDBB	lithium di-tert-butyl biphenyl
LiOH	lithium hydroxide
LiOOH	lithium peroxide
m	multiplet
M	molarity
m/z	mass/charge
(M + Na)	molecular weight + sodium
MBz	<i>para</i> -methoxybenzoyl
mCPBA	<i>meta</i> -chloroperoxybenzoic acid
Me	methyl
MeCN	acetonitrile
MeI	iodomethane
MeLi	methyl lithium

MeMgBr	methylmagnesium bromide
MeNO ₂	nitromethane
MeO	methoxy
MeOH	methanol
MeReO ₃	methyltrioxorhenium
Me ₂ CuLi	Gilman's reagent
Me ₂ S	dimethyl sulfide
Me ₃ S ⁺ I ⁻	trimethylsulfonium iodide
Me ₃ SiCl	trimethylsilyl chloride
Me ₃ SiOK	potassium trimethylsilanolate
(MeSO ₂) ₂ O	methanesulfonic anhydride
mg	milligram(s)
Mg	magnesium
MHz	megahertz
μL	microliter(s)
min	minute(s)
mL	milliliter(s)
mmol	millimole
mmHg	millimeters of mercury
MOM	methoxymethyl
MOMCl	chloromethyl methyl ether
MS	mass spectrometry

MsCl	methanesulfonyl chloride
MTO	methyltrioxorhenium
Na(AcO) ₃ BH	sodium triacetoxylborohydride
NaBH ₄	sodium borohydride
NaClO ₂	sodium chlorite
<i>n</i> -BuOLi	lithium <i>n</i> -butoxide
Na	sodium
NaH	sodium hydride
NaHCO ₃	sodium bicarbonate
NaHMDS	sodium 1,1,1,3,3,3-hexamethylsilazane
NaH ₂ PO ₄	sodium dihydrogen phosphate
NaHSO ₃	sodium bisulfite
NaIO ₄	sodium periodate
NaN ₃	sodium azide
NaOAc	sodium acetate
NaOH	sodium hydroxide
NaO- <i>t</i> Bu	sodium tert-butoxide
Na ₂ S ₄ ·H ₂ O	sodium sulfide hydrate
Na ₂ S ₈ ·9H ₂ O	sodium sulfide nonahydrate
Na ₂ SO ₄	sodium sulfate
NBS	<i>N</i> -bromosuccinimide
NFSI	<i>N</i> -fluorobenzenesulfonimide

NH ₂ OH·HCl	hydroxylamine hydrochloride
<i>n</i> -BuLi	<i>n</i> -butyllithium
NIS	<i>N</i> -iodosuccinimide
NMO	<i>N</i> -methylmorpholine- <i>N</i> -oxide
NMP	<i>N</i> -methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
O ₃	ozone
OsO ₄	osmium(VIII) oxide
Pd/C	palladium(0) on charcoal
Pd/CaCO ₃	palladium (0) on calcium carbonate Lindlar Catalyst
PdCl ₂ (dppf)	[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride
Pd(PPh ₃) ₄	tetrakis(triphenylphosphine)palladium (0)
Pd ₂ (dba) ₃	tris(dibenzylideneacetone)dipalladium (0)
[Pd(allyl)Cl] ₂	allylpalladium(II) chloride dimer
Ph	phenyl
Ph ₂ SiH ₂	diphenylsilane
Ph ₃ As	triphenylarsine
PhI(OAc) ₂	(diacetoxyiodo)benzene
PhMe	toluene
[Ph ₃ P] ₃ RuCl ₂	dichlorotris(triphenylphosphine)ruthenium(II)
Ph ₃ SiOReO ₃	triphenylsilyl perrhenate

PivCl	Pivaloyl chloride
PMe ₃	trimethylphosphine
POCl ₃	phosphorus(V) oxychloride
PPh ₃	triphenylphosphine
PPh ₃ AuCl	chloro(triphenylphosphine)gold(I)
PMB	<i>para</i> -methoxybenzyl
PMP	<i>para</i> -methoxyphenyl
ppm	parts per million
PPTS	pyridinium <i>p</i> -toluenesulfonate
PTSA	<i>para</i> -toluenesulfonic acid
<i>p</i> -ABSA	4-acetamidobenzenesulfonyl azide
<i>p</i> -Tol	<i>para</i> -tolyl
<i>p</i> -TsOH	<i>para</i> -toluenesulfonic acid
PtCl ₂	platinum(II) chloride
PvCl	pivaloyl chloride
Py	pyridine
[Rh(COD)Cl] ₂	chloro(1,5-cyclooctadiene)rhodium(I) dimer
RCM	ring-closing metathesis
Re ₂ O ₇	rhenium(VII) oxide
Rh ₂ (OAc) ₄	rhodium acetate
rt	room temperature

(<i>R</i>)-(p-tolyl) ₂ BINAP	(<i>R</i>)-(-)- <i>para</i> -toluenesulfinamide
s	singlet
SO ₃	sulfur trioxide
TBAF	tetrabutylammonium fluoride
TBAI	tetrabutylammonium iodide
<i>t</i> -BuLi	<i>tert</i> -butyl lithium
<i>t</i> -BuOH	<i>tert</i> -butanol
TBD	1,5,7-triazabicyclo[4.4.0]dec-5-ene
TBDPS	<i>tert</i> -butyldiphenylsilyl
TBDPSCI	<i>tert</i> -butyl(chloro)diphenylsilane
TBS	<i>tert</i> -butyldimethylsilyl
TBSCl	<i>tert</i> -butyldimethylsilyl chloride
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy, free radical
TES	triethylsilyl
TESCl	triethylsilyl chloride
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TiCl ₄	titanium(IV) chloride
TIPS	triisopropylsilyl
TIPSCI	chlorotriisopropylsilane
TMS	trimethylsilyl
TMSCl	trimethylsilyl chloride

TMSCHN_2	trimethylsilyldiazomethane
Ts	4-toluenesulfonyl
TsCl	4-toluenesulfonyl chloride
Z	zusammen
Zn	Zinc
ZrCl_4	zirconium tetrachloride
ZrHCp_2Cl	zirconocene chloride hydride (Schwartz's reagent)

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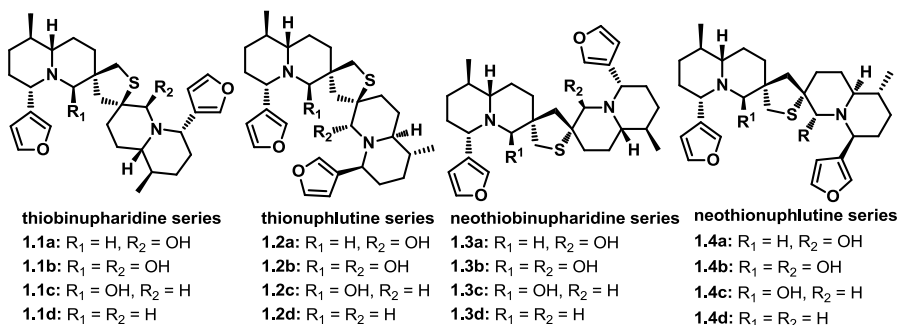
Chapter 1

Studies Towards the Total Synthesis of Nuphar Thiaspirane Alkaloids

1.1 Nuphar Thiaspirane Alkaloids Background

Nupharis Rhizoma was used as a tonic, diuretic, and treatment of blood stasis syndrome in Chinese and Japanese traditional medicine. Various alkaloids have been isolated from rhizome of *Nuphar japonicum* and *Nuphar pumilum* (T_{IMM.}) DC, including three types of dimeric sesquiterpene alkaloids in the thiobinupharidine, thionuphlutine, and neothiobinupharidine series (Figure 1.1.1). In 1965, Birnbaum corrected the structure of thiohemiaminal-type dimeric sesquiterpene neothiobinupharidine **1.3b**,¹ which had first been isolated by Achmatowicz a year earlier,² via X-ray crystallographic diffraction. In the 1970s, LaLonde extensively studied the structural elucidation of these dimeric sesquiterpene alkaloids, especially thiohemiaminal-type alkaloids, and also insightfully proposed their biogenesis from monomeric sesquiterpene congeners.³

Figure 1.1.1 Nuphar Thiaspirane Alkaloids



1.2 Biological Activities of Nuphar Thiaspirane Alkaloids

In general, alkaloids of botanical origin display a wide variety of unique and potent activities against disease targets; furthermore, they possess special promise as anticancer agents.⁴ A recent study found that 57% of the 155 antineoplastic agents marketed in Western countries since the 1940s have been either unmodified natural products (25 compounds, 16%) or semi-synthetic derivatives of natural products (48 compounds, 41%).⁵

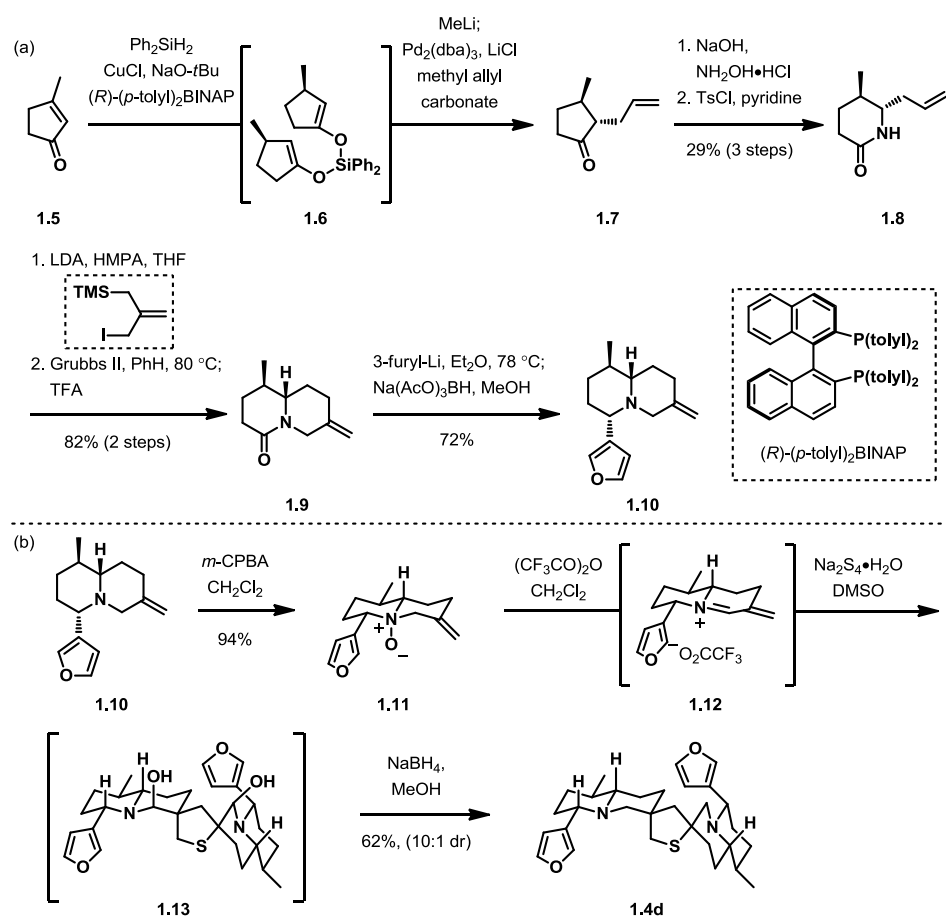
Despite the long history of these nuphar thiaspirane alkaloids, the remarkable biological activities of these dimeric nuphar thiaspirane alkaloids were not detected until the 2000s. These include antibacterial, antifungal, immunosuppressive, and potent *in vitro* cytotoxicity against U937 human leukemia, B16F10 mouse melanoma, and HT1080 human fibroblast cell lines.⁶ Distinctive nuphar dimers 6-hydroxythiobinupharidine (**1.1a**), 6,6'-dihydroxythiobiunpharidine (**1.1b**), and 6-hydroxythionuphlutine B (**1.2a**) have been shown to inhibit invasion of B16 murine melanoma cells across collagen-coated filters *in vitro* with IC₅₀ values of 29 nM, 87 nM, and 360 nM, respectively.⁷ Recently, Gopas and co-workers reported that methanolic extracts from *Nuphar lutea* inhibit nuclear factor κ B (NF κ B) and exhibit synergistic effects with conventional chemotherapy.⁸ NF κ B signaling has been implicated in oncogenesis and tumor progression, inhibition of which has enabled the search for its specific target and applications against cancer and inflammation.

1.3 Previous Syntheses of Nuphar Thiaspirane Alkaloids

To date, only one synthesis of one member from this family of natural products has been reported. In 2013, Shenvi and co-workers reported an eight-step synthesis of (-)-neothiobinupharidine (**1.4d**), an isomer that has never been isolated from natural sources (Scheme 1.3.1).⁹ Quinolizidine monomer **1.10** was elegantly prepared from 3-

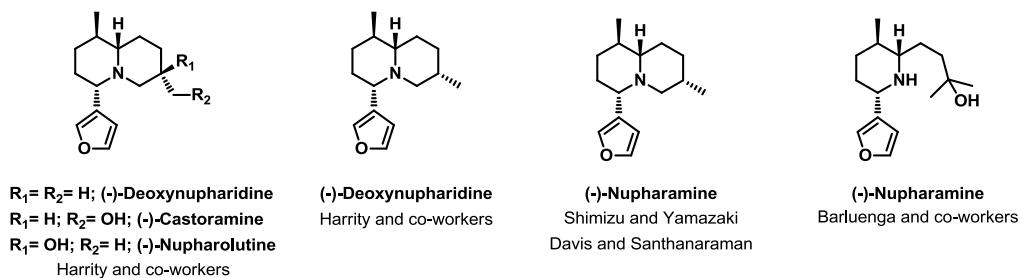
methylcyclopentenone **1.5** through a conjugate reduction-allylation sequence to form cyclopentane **1.7**. Formation of the quinolizidine core **1.9** was completed by ring closing metathesis (RCM) followed by protodesilylation. Dimerization of the quinolizidine monomers **1.10** in the presence of sodium tetrasulfide produced **1.4d** in 62% yield stereoselectively. Unfortunately, the authors did not report any biological activity of their synthetic isomer.

Scheme 1.3.1 Shenvi's Total Synthesis of (-)-Neothiobinupharidine



There have been various syntheses of monomeric sesquiterpene alkaloids by various groups shown in Figure 1.3.1 (*vide infra*).¹⁰

Figure 1.3.1 Monomeric Sesquiterpene Alkaloid Syntheses

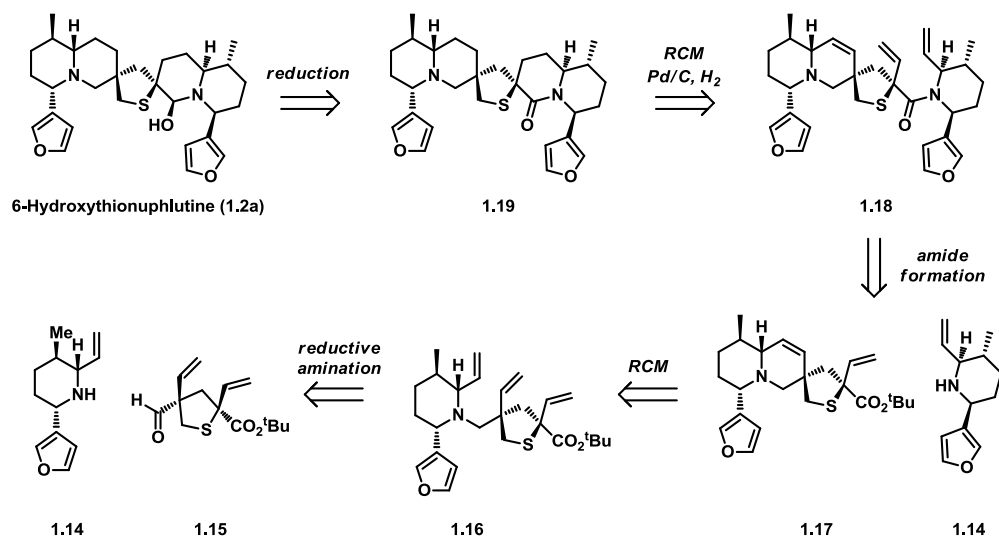


A new strategy is necessary to access other members of the family to provide the significant quantities of the natural isomers, which would be necessary for studies towards the elucidation of their biological targets and mechanism of action, both of which are absent from current literature.

1.4 Initial Synthetic Plan

In devising an overall approach to synthesize the four classes of nuphar thiaspirane alkaloids, we became interested in developing a general strategy of coupling a piperidine to one of four tetrahydrothiophene isomers, shown in Scheme 1.4.1. Initial coupling of our tetrahydrothiophene **1.15** with piperidine **1.14** through reductive amination would deliver **1.16**, followed by RCM to form the first quinolizidine core **1.17**. To gain access to **1.18**, amide bond formation between **1.17** and piperidine **1.14** would be implemented. To form the second quinolizidine core, a RCM followed by hydrogenation would yield **1.19**. Finally, reduction of **1.19** would deliver our desired nuphar thiaspirane alkaloid, 6-hydroxythionupharlutine **1.2a**.

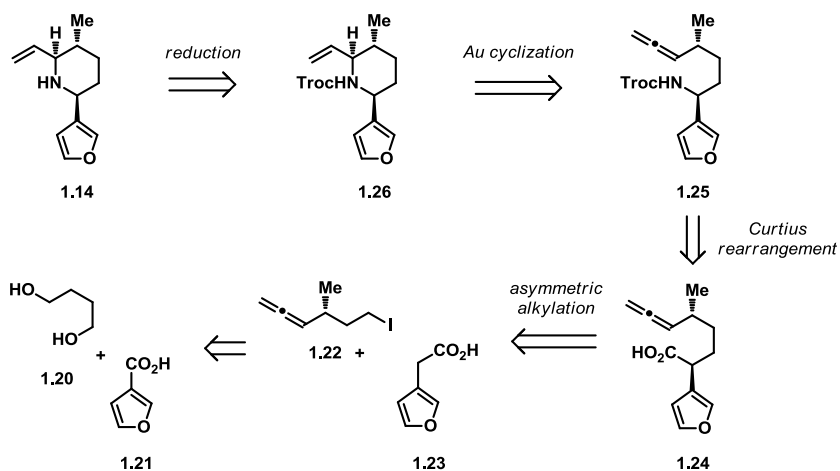
Scheme 1.4.1 Synthetic Plan of Nuphar Thiaspirane Alkaloids



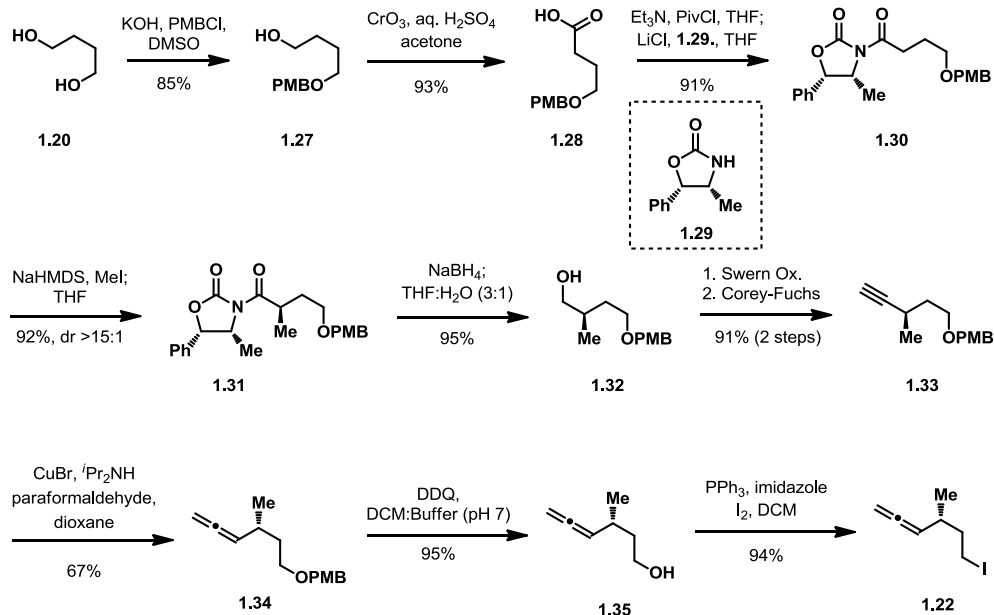
1.5 1st Generation Synthesis of Piperidine 1.14

In order to implement the final stages of our synthetic strategy, we conceived a strategy to synthesize piperidine **1.14**. We planned to use an asymmetric alkylation methodology, devised in the Zakarian group, coupling allene iodide **1.22** with 3-furylacetic acid **1.23** forming carboxylic acid **1.24**.¹¹ Curtius rearrangement would deliver carbamate **1.25**. A key gold cyclization followed by protecting group removal would deliver **1.14**.

Scheme 1.5.1 Synthetic Plan of Piperidine **1.14**

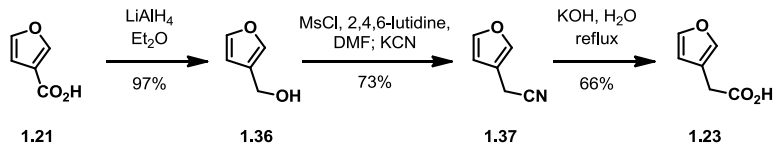


Scheme 1.5.2 Synthesis of Allene Iodide **1.22**



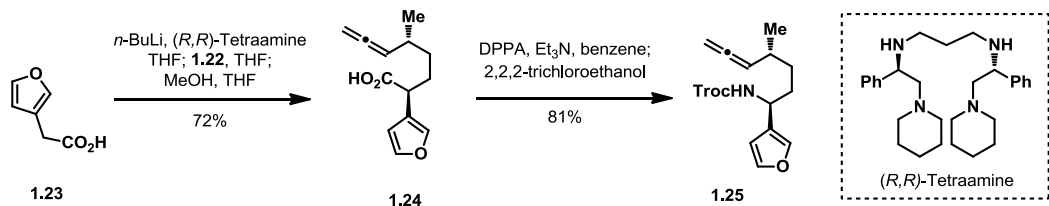
The synthesis of the allene iodide **1.22**, shown in Scheme 1.5.2, began from commercially available 1,4-butanediol **1.20**, which was mono-PMB protected to afford the corresponding primary alcohol **1.27**, in 85% yield.¹² After protection, the resultant alcohol was oxidized by means of a Jones oxidation yielding carboxylic acid **1.28**, and then coupled with oxazolidinones **1.29**, in 85% yield over two steps.¹³ Methylation of *N*-acyl oxazolidione **1.30** formed **1.31** in high yield and diastereoselectivity. Reduction of **1.31** with NaBH_4 delivered primary alcohol **1.32** in 95% and the oxazolidinone **1.29** was quantitatively recovered. Swern oxidation followed by a Corey-Fuchs reaction provided alkyne **1.33** in 91% yield over two steps.¹⁴ Allene **1.34** was formed using paraformaldehyde in a one carbon homologation reaction.¹⁵ Deprotection of PMB followed by an Appel reaction produced allene iodide **1.22**.^{13,16}

Scheme 1.5.3 Synthesis of 3-Furylacetic Acid **1.23**



Formation of 3-furylacetic acid **1.23** was initiated via reduction of commercially available 3-furanoic acid **1.21** with LiAlH_4 , which delivered primary alcohol **1.36** (Scheme 1.5.3). Alcohol **1.36** was first mesylated, followed by cyanide addition to form nitrile **1.37**. Treatment of nitrile **1.37** with potassium hydroxide under refluxing conditions produced 3-furylacetic acid **1.23**, in 47% yield over three steps.¹⁷

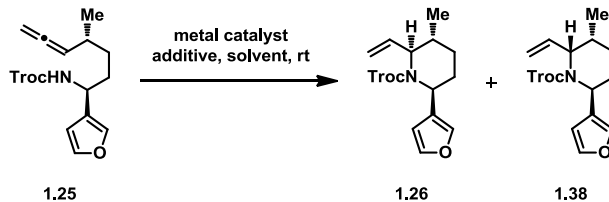
Scheme 1.5.4 Asymmetric Alkylation & Curtius Rearrangement



Utilizing chemistry developed in the Zakarian group, 3-furylacetic acid **1.23** was coupled with allene iodide **1.22** through an asymmetric alkylation with (*R,R*)-tetraamine, delivering carboxylic acid **1.24** in good yield and excellent selectivity.¹¹ Curtius rearrangement formed carbamate **1.25** in 81% yield.¹⁸

An initial screen of metals was performed to assess the ability to cyclize carbamate **1.25** to piperidine **1.26** (Table 1.5.1). Cyclization was not observed when using rhodium, iridium, iron, silver, platinum, or palladium¹⁹ (entries 1-9) as our metal catalyst. When carbamate **1.25** was subjected to PPh_3AuCl , with silver triflate as an additive, cyclization was observed in good yield but with no stereoselectivity (entries 12-13).²⁰

Table 1.5.1 Metal Screen: Piperidine **1.26** Cyclization

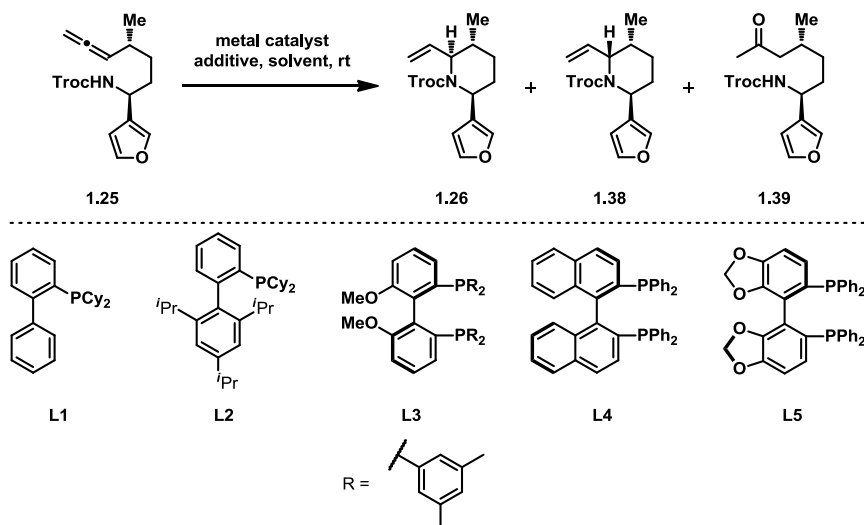


Entry	Metal (mol %)	Additive (mol %)	Solvent	Yield
1	[Rh(COD)Cl] ₂ (1.0)	DPEphos (3.0)	EtOH:DCE	0% ^a
2	[Ir(COD)Cl] ₂ (1.0)	DPEphos (3.0)	THF	0%
3	FeCl ₃ ·6H ₂ O (10.0)		CH ₂ Cl ₂	0%
4	AgOTf (50.0)		toluene	0%
5	AgBF ₄ (50.0)		toluene	0%
6	AgClO ₄ (50.0)		toluene	0%
7	PtCl ₂ (10.0)		CH ₂ Cl ₂	0%
8	[Pd(allyl)Cl] ₂ (10.0)	dppf (20.0)	THF	0% ^a
9	PdCl ₂ (dppf) (10.0)		THF	0%
10	AuCl ₃ (5.0)	AgClO ₄ (10.0)	xylenes	0%
11	AuCl ₃ (5.0)	AgClO ₄ (10.0)	CH ₂ Cl ₂	0%
12	PPh ₃ AuCl (20.0)	AgOTf (40.0)	toluene	68%, dr 1:1
13	PPh ₃ AuCl (30.0)	AgOTf (60.0)	CH ₂ Cl ₂	50%, dr 1:1

(a) **1.1** was consumed, formation of an unknown product.

We sought to improve our conversion and diastereoselectivity by using ligands to assist in our gold cyclization reaction. Phosphine ligands JohnPhos (**L1**), XPhos (**L2**), and (*R*)-SegPhos (**L5**) were tested but no conversion to the cyclized piperidine was observed (Table 1.5.2, entries 1-2, 5). Chiral ligand MeOBIPHEP (**L3**) was used and led to full conversion but only formed the non-cyclized methyl ketone **1.39** (entry 3). Among the phosphine ligands, usage of (*R*)-BINAP led to full conversion, forming piperidine **1.26** and **1.38** as the major products, along with a minor amount of methyl ketone **1.39** (entry 4). Unfortunately there was no improvement of diastereoselectivity with the conditions used.

Table 1.5.2 Au-Ligand Screen^a



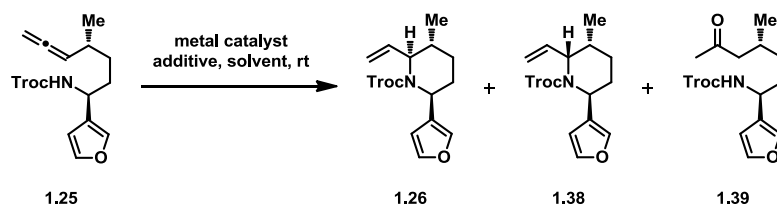
Entry	Au source (mol %)	Additive (mol %)	Solvent	Conversion	1.14:1.38:1.39
1	AuNTf ₂ ·L ₁ (10.0) ^b	AgOTf (10.0)	dioxane	0%	
2	AuNTf ₂ ·L ₂ (10.0) ^c	AgOTf (10.0)	dioxane	0%	
3	AuCl·L ₃ (5.0) ^d	AgOTf (10.0)	toluene	100%	0:0:1
4	AuCl·L ₄ (25.0) ^e	AgOTf (50.0)	CH ₂ Cl ₂	100%	2:2:1
5	AuCl·L ₅ (25.0) ^f	AgOTf (50.0)	toluene	0%	

(a) Standard conditions: solvent (0.5 M) at room temp. (b) L1: Cyclohexyl JohnPhos (c) L2: XPhos (d) L3: (R)-3,5-Xyl-MeOBIPHEP (e) L4: (R)-BINAP (f) L5: (R)-SegPhos

Further reaction optimization of the gold cyclization was completed in order to improve the diastereoselectivity and minimize the methyl ketone **1.39** by-product. Under optimized conditions, 20 mol % of AuCl[(R)-BINAP], 80 mol % of silver tetrafluoroborate (AgBF₄) and 4 Å molecular sieves, in a solvent mixture of toluene and dichloromethane are required for affording the piperidine **1.26** albeit in modest yield and selectivity (Table 1.5.3, entry 9). Variation of solvents, toluene:acetonitrile and dioxane, led to no product formation (entries 1, 4). Reduction of gold and silver loading led to reduced yields (entries 2-3). Using dichloromethane as the only solvent led to good yield, but poor diastereoselectivity and large amount of methyl ketone **1.39** formation (entry 5). In attempts to ensure dry reaction

conditions, 4Å MS were added, which led to a reduction in the amount of methyl ketone **1.39**? but low diastereoselectivity remained a problem (entries 6-7).

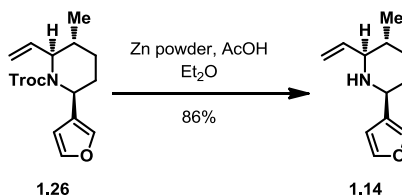
Table 1.5.3 Reaction Optimization



Entry	AuCl[(<i>R</i>)-BINAP]	AgBF ₄	Additive	Solvent	Yield	1.14:1.38:1.39
1 ^a	20 mol %	40 mol %		toluene:CH ₃ CN	0%	
2	15 mol %	30 mol %		CH ₂ Cl ₂	35%	1.7:1:1
3	15 mol %	30 mol %		toluene:CH ₂ Cl ₂	49%	2.8:1:1
4	15 mol %	30 mol %		dioxane	0%	
5	20 mol %	40 mol %		CH ₂ Cl ₂	85%	1:1:0.7
6	20 mol %	40 mol %	4Å MS	CH ₂ Cl ₂	64%	1:1:0.4
7	20 mol %	40 mol %	4Å MS	toluene:CH ₂ Cl ₂	89%	1:1:0.6
8	20 mol %	40 mol %	4Å MS, LiCl	toluene:CH ₂ Cl ₂	0%	
9	20 mol %	80 mol %	4Å MS	toluene:CH ₂ Cl ₂	71%	2.1:1:1.3

(a) Standard conditions: **1.25** is added to a mixture of AuCl[(*R*)-BINAP] and AgBF₄ in solvent at room temperature. (b) reaction was heated to 45 °C.

Scheme 1.5.5 Formation of Piperidine **1.14**

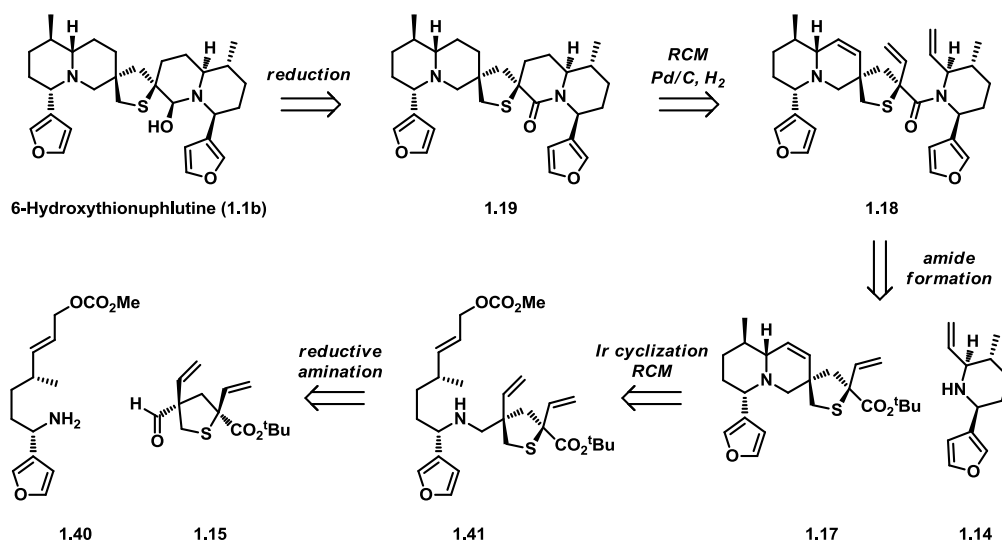


Deprotection of carbamate **1.26** with zinc in acetic acid and diethyl ether provided piperidine **1.14** in high yield (Scheme 1.5.5). Due to the high number of steps and lack of selectivity in the key gold cyclization, this plan to synthesize piperidine **1.14** was revised.

1.6 Revised Synthetic Plan

In revising our overall approach to synthesize the four classes of nuphar thiaspirane alkaloids, we planned to use an iridium-catalyzed allylic cyclization as our key step to form the quinolizidine cores, shown in Scheme 1.6.1. Initial coupling of our tetrahydrothiophene **1.15** with amine **1.40** through reductive amination would deliver **1.41**. A key iridium-catalyzed allylic cyclization followed by ring closing metathesis would form the first quinolizidine core **1.17**. To gain access to **1.18**, amide bond formation between **1.17** and piperidine **1.14** would be implemented. To form the second quinolizidine core, a RCM followed by hydrogenation would yield **1.19**. Finally, reduction of **1.19** would deliver the desired thiaspirane, 6-hydroxythionuphlutine **1.1b**.

Scheme 1.6.1 Synthetic Plan of Nuphar Thiaspirane Alkaloids

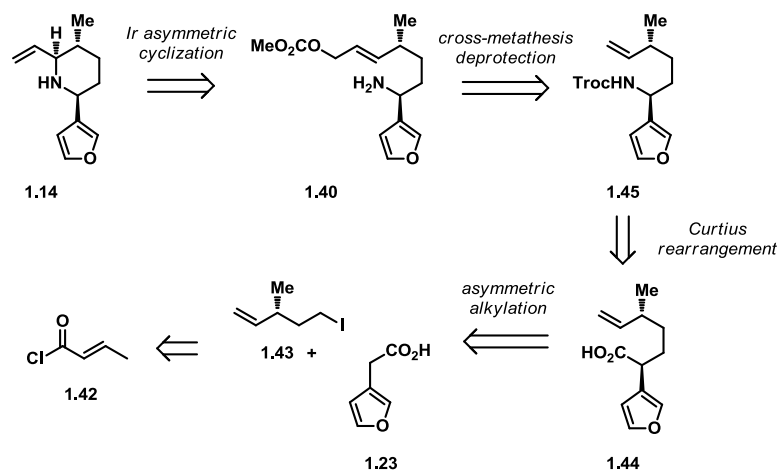


1.7 2nd Generation Synthesis of Piperidine 1.14

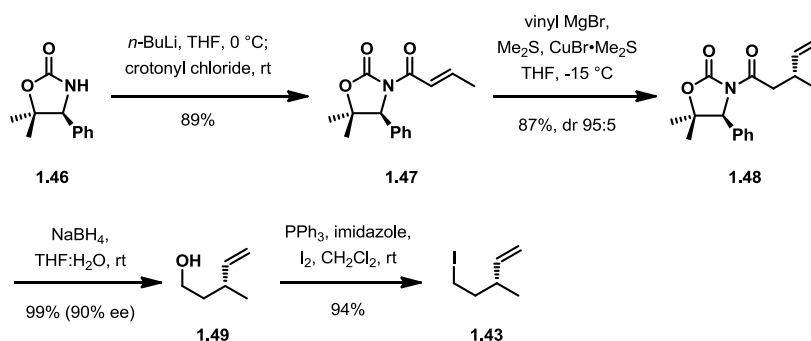
Due to the high step count and low overall yield for our initial synthesis of piperidine **1.14**, a revision was proposed. In devising a new approach, we planned to form piperidine **1.14** in a similar manner to the first generation synthesis. We varied our plan by using an

iridium-catalyzed allylic cyclization of amine **1.40** to produce piperidine **1.14** (Scheme 1.7.1).²¹

Scheme 1.7.1 Revised Synthetic Plan of Piperidine **1.14**

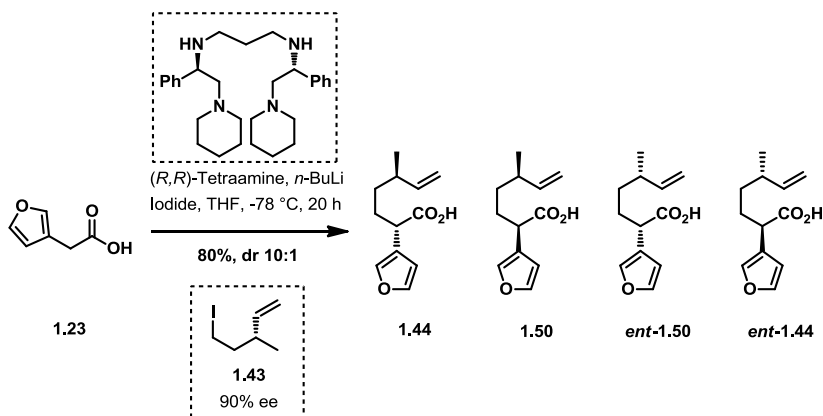


Scheme 1.7.2 Synthesis of Alkyl Iodide **1.43**



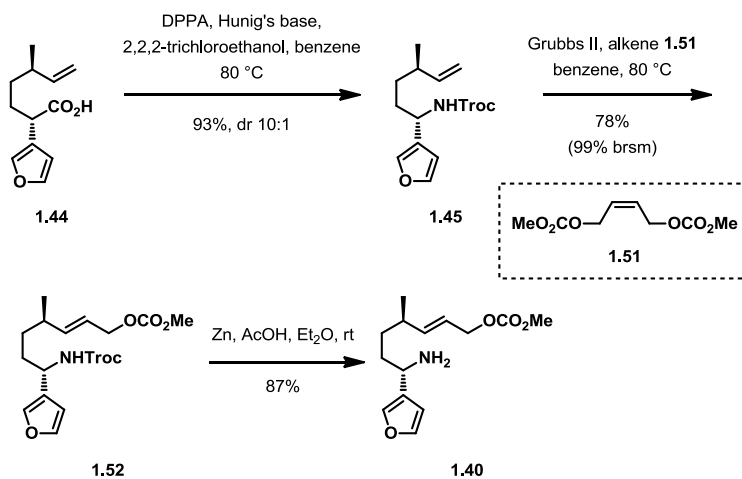
Acylation of oxazolidione **1.46** with crotonyl chloride delivered *N*-acyl oxazolidione **1.47** in high yield. A 1,4-addition of vinyl cuprate produced terminal alkene **1.48** in 87% yield and high diastereoselectivity.²² Reduction with NaBH_4 followed by an Appel reaction produced the alkene iodide **1.43**. Thus, the synthesis of the iodide was completed in 5 steps, an overall 81% yield in 90% enantiomeric excess.

Scheme 1.7.3 Asymmetric Alkylation



An asymmetric alkylation of iodide **1.43** with 3-furylacetic acid **1.23** using (R,R) -tetraamine produced our desired addition producing **1.44** in high yield with great stereoselectivity in addition with the remaining three inseparable isomers. The reaction increased the enantiomeric excess of our desired product **1.44** over its enantiomer *ent*-**1.44**.

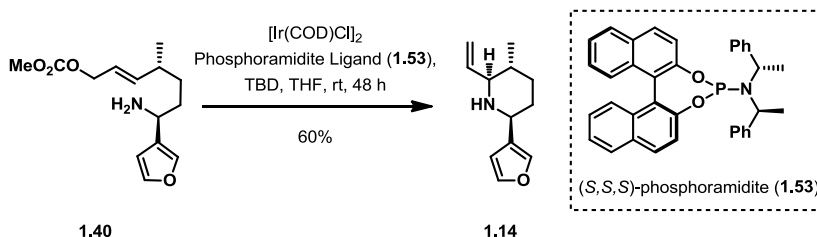
Scheme 1.7.4 Synthesis of Primary Amine 1.40



The sterically bulky Hünig's base proved to be the key in the Curtius rearrangement of acid **1.44** by completely eliminating epimerization during the formation of carbamate **1.45**. The sterically smaller triethylamine leads to a partial epimerization, reducing dr from 10:1 to 3:1. Cross-metathesis proved uneventful, providing carbonate **1.52** in good yield, with the

starting material making up the remaining mass balance.²³ Removal of the Troc protecting group with zinc powder led to key primary amine **1.40**.

Scheme 1.7.5 Iridium-Catalyzed Allylic Cyclization

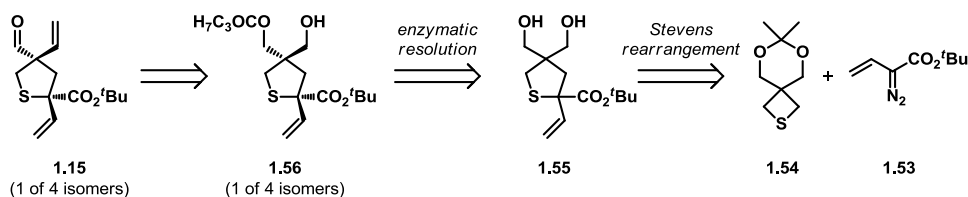


Cyclization of primary amine **1.40** via iridium catalysis under Helmchen conditions with phosphoramidite ligand²⁴ **1.53** provided piperidine **1.14** in good yield and excellent selectivity.²⁵

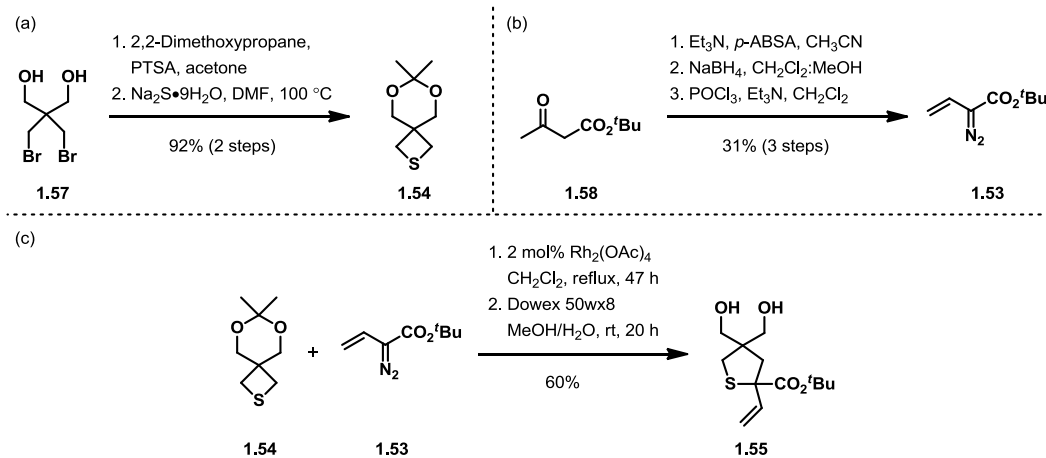
1.8 Synthesis of Tetrahydrothiophene **1.15**

Our synthetic strategy was guided by the decision to pursue all four types of dimeric sesquiterpene alkaloids, assembled from one of four tetrasubstituted tetrahydrothiophene isomers. Preparation of tetrahydrothiophene **1.15** will commence with a Stevens rearrangement between thietane **1.54** and diazo **1.53** forming the initial tetrahydrothiophene core **1.55**.²⁶ To access all four isomers, we plan to use enzymatic resolution followed by multiple steps to achieve the desired coupling partner **1.15**.

Scheme 1.8.1 Synthetic Plan of Tetrahydrothiophene **1.15**

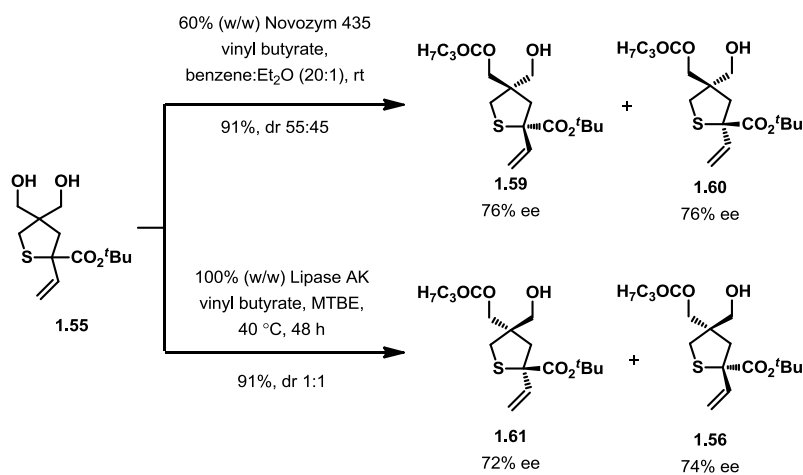


Scheme 1.8.2 Synthesis of Tetrahydrothiophene **1.55**



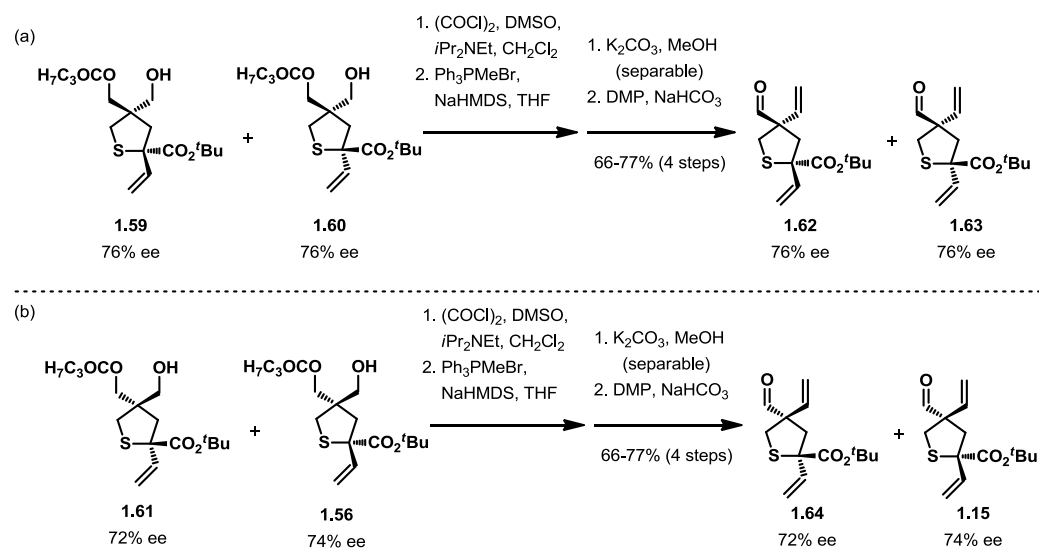
Thietane **1.54** was prepared from diol **1.57** by diol protection followed by thio-substitution with sodium sulfide, depicted in Scheme 1.8.2a.²⁷ Commercially available *tert*-butyl acetoacetate **1.58** was subjected to diazo formation with *p*-ABSA, followed by reduction with NaBH₄, and elimination to deliver diazo **1.53** in three steps (Scheme 1.8.2b).²⁸ Diol **1.55** was prepared in two steps via Stevens rearrangement of **1.54** with **1.53** and subsequent removal of acetone (Scheme 1.8.2c)

Scheme 1.8.3 Enzymatic Resolution of Tetrahydrothiophene **1.55**



Desymmetrization is a powerful tool for the preparation of enantiomerically pure substrates. Desymmetrization of one prochiral carbon center in a racemic substrate would give two diastereomers with *de facto* enantiomeric purity. Although the copper-catalyzed desymmetrization reaction gave no better than 40% ee,²⁹ enzyme-mediated reaction afforded the desired diastereomers **1.59** and **1.60** after optimization. In presence of Novozym 435, diastereomers **1.59** and **1.60** could be isolated in 91% combined yield with a nearly 1:1 diastereomeric ratio and 76% ee (Scheme 1.8.3). In addition, **1.61** and **1.56** could also be efficiently prepared using enzyme lipase AK. Thus, four isomers of tetrahydrothiophenes could be feasibly accessed by choice of enzyme (Scheme 1.8.3).

Scheme 1.8.4 Synthesis of Tetrahydrothiophenes – 4 Isomers



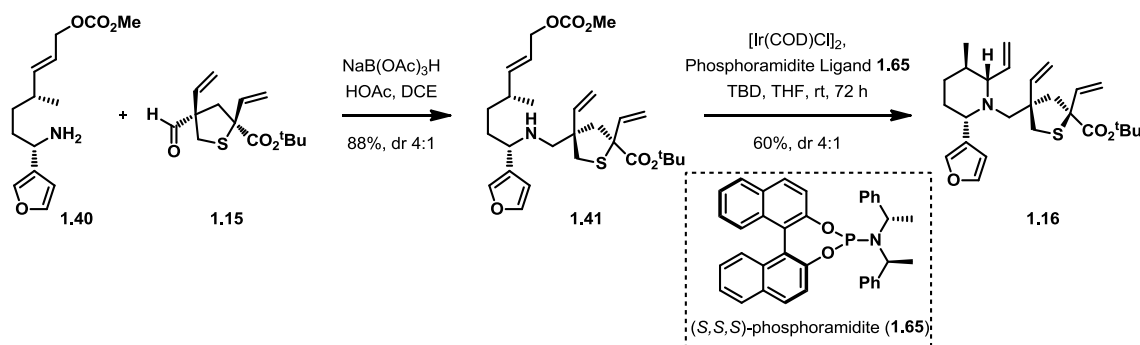
To prepare the final four tetrahydrothiophene isomers, the enzymatically resolved tetrahydrothiophenes **1.56** and **1.59-1.61** were subjected to Swern oxidation followed by Wittig olefination (Scheme 1.8.4–b). The tetrahydrothiophenes were subjected to deprotection and at this point isomers were separated by column chromatography. Dess-

Martin oxidation produced the desired tetrahydrothiophene isomers: **1.62**, **1.63**, **1.64**, and **1.15** in a total of four steps, in good yield and enantiomeric excess.

1.9 Synthesis of Nuphar Thiaspirane Alkaloids

Obtaining key fragments, amine **1.5** and all tetrahydrothiophene isomers (**1.15**, **1.62-1.64**), permitted the total synthesis of nuphar thiaspirane alkaloids to proceed via coupling of fragments.

Scheme 1.9.1 Formation of Quinolizidone Core

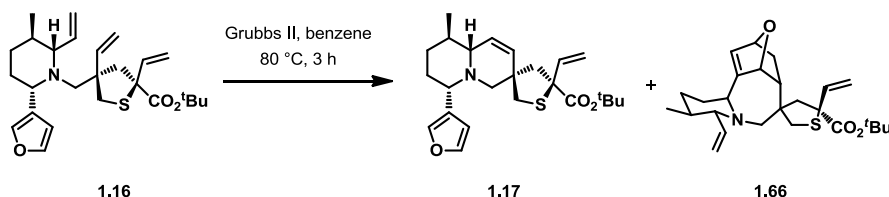


Reductive amination of primary amine **1.40** with aldehyde **1.15** provided the coupled fragment **1.41** in high yield and good diastereoselectivity (Scheme 1.9.1). Our first key iridium allylic cyclization proved to be uneventful, delivering piperidine **1.16** in good yield and complete stereoselectivity. At this point diastereomers could be separated and isomer **1.16** was subjected to RCM conditions.

A fast screen of metal catalysts revealed that Grubbs 2nd generation catalyst led to full conversion (Table 1.9.1, entry 1). Hoveyda-Grubbs 2nd generation (HGII) and Schrock catalysts were also screened but led to incomplete conversion (entries 2-3). Extended reaction times led to a greater amount of Diels-Alder by-product **1.66** (entry 4). Lowering reaction time to 6 hours led to full conversion with a 52% of desired quinolizidine **1.17**

(entry 5). Due to the high catalyst loading, it was proposed that the GII catalyst was forming a tightly bound intermediate with the substrate after one turnover of the catalyst. In an attempt to achieve full conversion to the desired quinolizidine **1.17** and lower the catalyst loading, ethylene was used to replace argon as the reaction atmosphere but this proved to be unfruitful (entry 7).

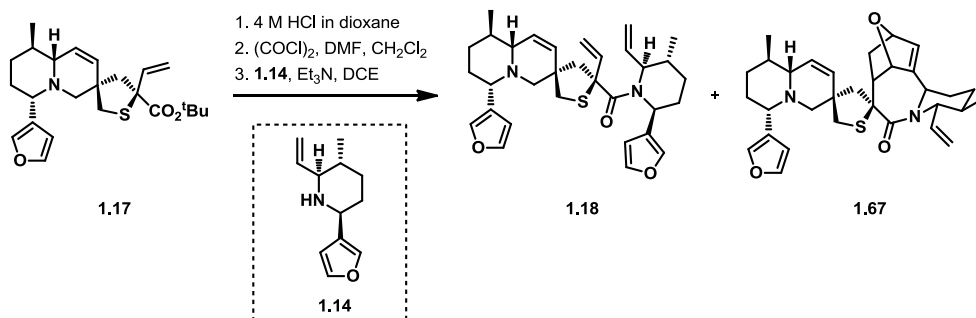
Table 1.9.1 Ring-Closing Metathesis^a



Entry	Catalyst (mol %)	Solvent	Time (h)	Conversion	Yield	1.17:1.66
1	GII ^b (37.5)	benzene	24	100%	-	1:1
2	HGII ^c (37.5)	benzene	24	84%	-	1.3:1
3	Schrock (37.5)	benzene	12	50%	-	0:1
4	GII (30.0)	benzene	14	100%	74%	1.6:1
5	GII (50.0)	benzene	6	100%	58%	10:1
6	GII (50.0)	benzene	3	100%	56%	10:1
7 ^d	GII (25.0)	benzene	8	55%	30%	5:1

(a) Standard conditions: **1.16** in degassed benzene (0.01 M) in a sealed flask at 80 °C. (b) GII: Grubbs 2nd generation catalyst. (c) HGII: Hoveyda Grubbs 2nd generation catalyst. (d) reaction run under ethylene atmosphere.

Scheme 1.9.2 Amide Bond Formation



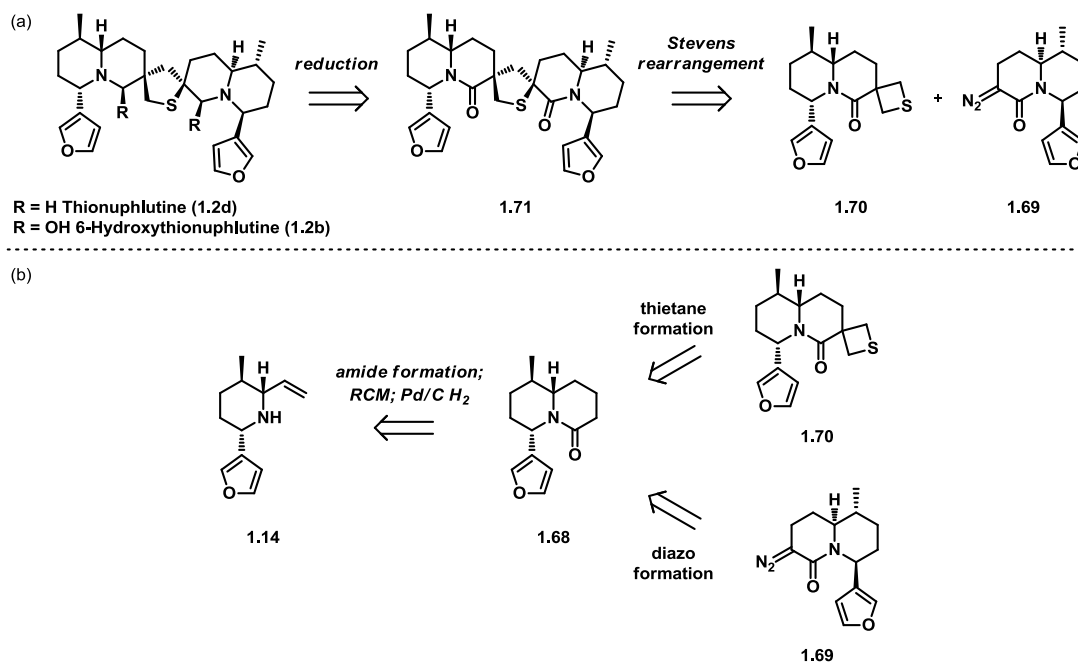
Advancing the synthesis, quinolizidine **1.17** was subjected to saponification in quantitative yield (Scheme 1.9.2). A screen of peptide bond forming reactions was conducted, including EDC/HOBt, DCC, EDC/DMAP, HATU, and HBTU, but no product formation was observed. Treatment of the acid with oxalyl chloride proved successful in preparing the acid chloride. Amide bond formation was examined with treatment of the acid chloride, piperidine **1.17**, and triethylamine in high concentration. The reaction was screened at various temperatures and times, but led exclusively to the undesired Diels-Alder byproduct **1.67** due to the Thorpe-Ingold effect. Unable to circumvent this unwanted side-product, the synthetic route was abandoned.

1.10 Revised Synthetic Plan of Nuphar Thiaspirane Alkaloids

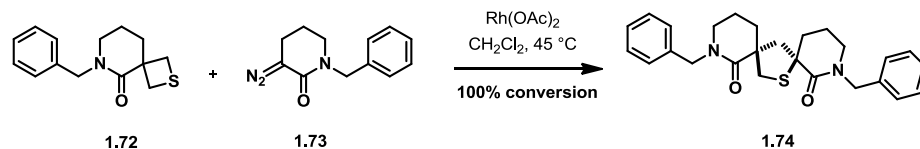
Revising our synthetic plan, formation of thietane **1.70** and diazo **1.69** could be formed from a common quinolizondine **1.68** intermediate (Scheme 1.10.1b). These two quinolizidines **1.69** and **1.70** could then be subjected to a Stevens rearrangement to deliver the bis-amide thioalkaloid **1.711** (Scheme 1.10.1a). Simple reduction could afford the bis-hemiaminal **1.2b** or the fully reduced **1.2d**.

To test the key Stevens rearrangement, a model reaction of thietane **1.72** and diazo lactam **1.73** was attempted. In the presence of catalytic $\text{Rh}_2(\text{OAc})_4$, the reaction of thietane **1.72** with diazo **1.73** smoothly afforded the desired thiaspirane **1.74** in full conversion (Scheme 1.10.2) as a single isomer.

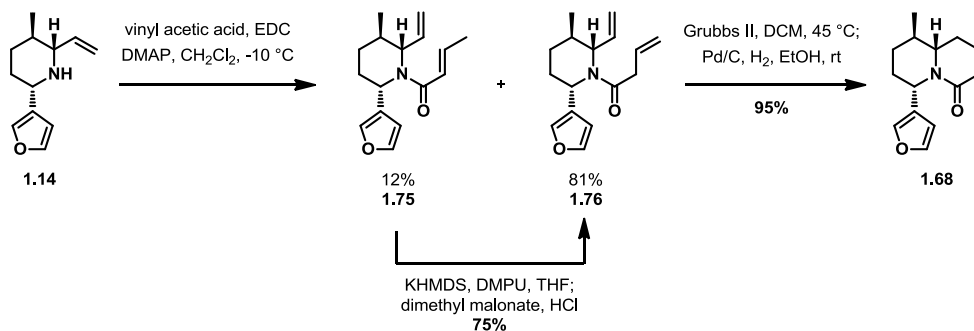
Scheme 1.10.1 Revised Synthetic Plan



Scheme 1.10.2 Stevens Rearrangement Model Reaction



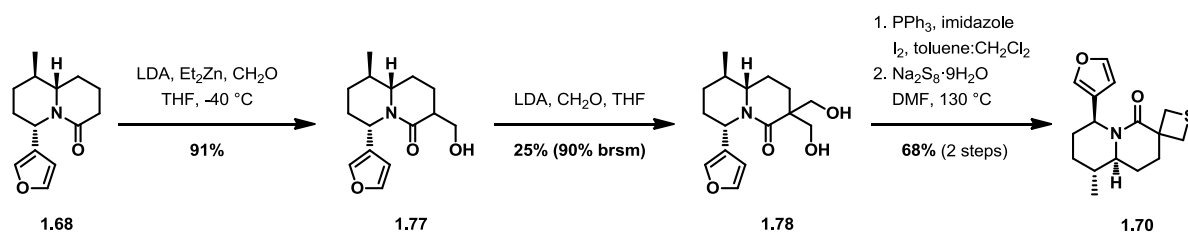
Scheme 1.10.3 Synthesis of Quinolizidine Core 1.68



Synthesis of quinolizidine **1.68** was completed in two steps from piperidine **1.14** (Scheme 1.10.3). Amide bond formation took place upon treatment of piperidine **1.14** with vinyl acetic acid, EDC, and DMAP in good yield. A small amount of isomerization to the

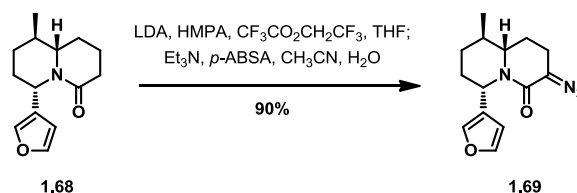
α,β -unsaturated amide **1.75** was observed, but was easily transformed back to the desired unconjugated product **1.76** upon treatment with KHMDS and quenching with dimethyl malonate in 75% yield.³⁰ RCM followed by hydrogenation proved uneventful, forming the quinolizidine core **1.68** in 95% yield.

Scheme 1.10.4 Synthesis of Thietane **1.70**



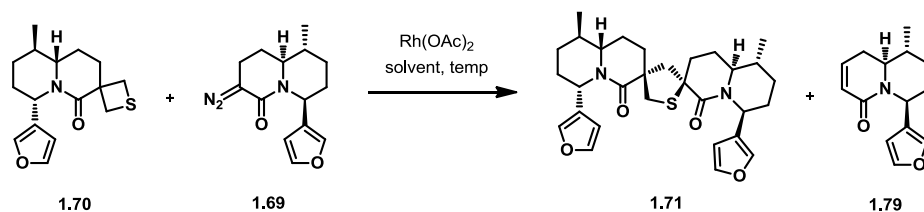
The initial aldol reaction began with the treatment of quinolizidine **1.68** with LDA and diethyl zinc, forming the zinc enolate. A solution of formaldehyde in THF was added, providing alcohol **1.77** in high yield (Scheme 1.10.4). An additional aldol was performed, but led to incomplete conversion, forming diol **1.78** in modest yield while retaining the remaining mixture as starting material **1.77**. Thietane formation proved to be successful with treatment of diol **1.78** by iodination followed by thio-substitution supplying thietane **1.70** in good yield over two steps.

Scheme 1.10.5 Synthesis of Diazo **1.69**



Next the α -diazo amide **1.69** was prepared via diazo transfer with use of *para*-acetamidobenzenesulfonyl azide (*p*-ABSA) from quinolizidine **1.68** (Scheme 1.10.5).³¹

Table 1.10.1 Stevens Rearrangement^a



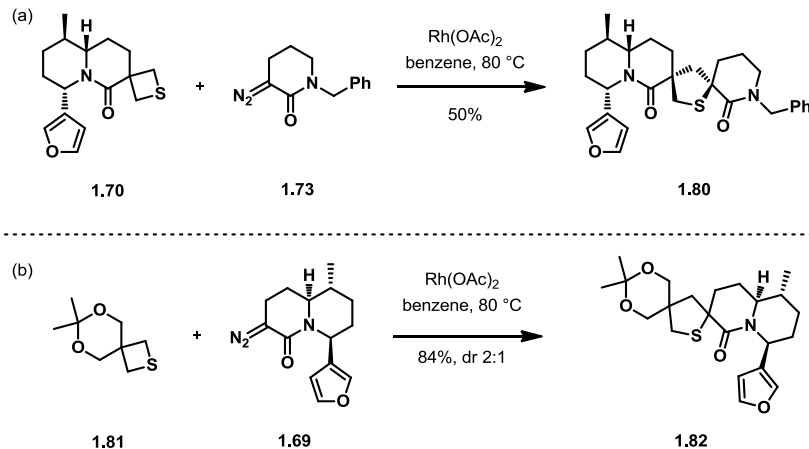
Entry	Rh(OAc) ₂	Solvent	Temp	Yield	34:1.8:1.7
1 ^b	25 mol %	CH ₂ Cl ₂	45 °C	0%	1.5:0:1
2 ^c	25 mol %	CH ₂ Cl ₂	45 °C	0%	1.5:0:0
3 ^d	25 mol%	DCE	90 °C	0% ₂	1.5:0:0

(a) Standard conditions: **1.70** (1.5 equiv), **1.69** (1.0 equiv), in DCM (0.05 M). (b) addition of diazo **1.69** over 1.5 h. (c) addition of diazo **1.69** over 3.5 h. (d) addition of diazo **1.69** over 16 h.

The key Stevens rearrangement was tested next with thietane **1.70** and diazo **1.69**. No product formation was observed when diazo **1.69** was added over 1.5 h to a solution of thietane **1.70** and Rh₂(OAc)₄ in dichloromethane at reflux (Table 1.10.1, entry 1). Formation of α,β -conjugated lactam **1.79** was exclusively observed along with unreacted thietane **1.70**. Extending addition time from 1.5 h to 3.5 h of diazo **1.69** reduced β -hydride elimination but no product formation was observed (entry 2). Increasing temperature to 90 °C and addition time to 16 h did not produce product **1.71** (entry 3).

Due to lack of product formation from the Stevens rearrangement, a new late-stage model was performed (Scheme 1.10.6). The model systems were to test reactivity of both thietane **1.70** and diazo **1.69**. Thietane **1.70** was reacted with model diazo **1.73** with Rh₂(OAc)₄ in refluxing benzene (Scheme 1.10.6a). Formation of product **1.80** was observed in 50% yield with 1 diastereomer observed. Next diazo **1.69** was reacted with model thietane **1.81** with Rh₂(OAc)₄ in refluxing benzene (Scheme 1.10.6b). Again, formation of product **1.82** was observed in high yield with a dr 2:1.

Scheme 1.10.6 Stevens Rearrangement: Late Stage Model

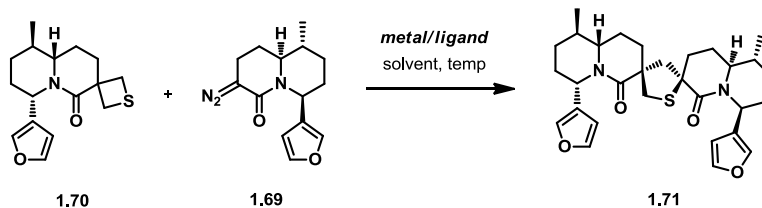


With these results (*vide supra*), we hypothesized that both the thietane **1.70** and diazo **1.69** are reactive and can undergo the Stevens rearrangement; however, the steric bulk in both compounds may lead to slow reactivity when coupling both together. We have observed that different metal/ligand combinations during Stevens rearrangement lead to different results be it higher and some times lower yields in the formation of thietanes. With the absence of desired thietane formation currently with $\text{Rh}_2(\text{OAc})_4$, new studies will need to be performed.

1-11 Future Studies

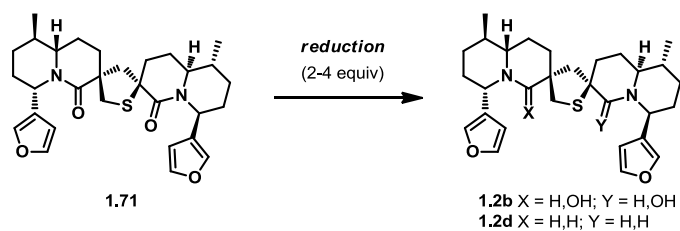
Future studies will concentrate on screening metal/ligand combinations to deliver the desired Stevens rearrangement (Scheme 1.11.1). Metals such as rhodium, ruthenium, copper, and iridium have been used in Stevens rearrangements successfully.

Scheme 1.11.1 Future Stevens Rearrangement Studies



Additional studies will include selective reduction to obtain multiple nuphar alkaloids (Scheme 1.11.2).

Scheme 1.11.2 Future Stevens Rearrangement Studies



Chapter 2

A Concise Asymmetric Total Synthesis of (+)-Brevisamide

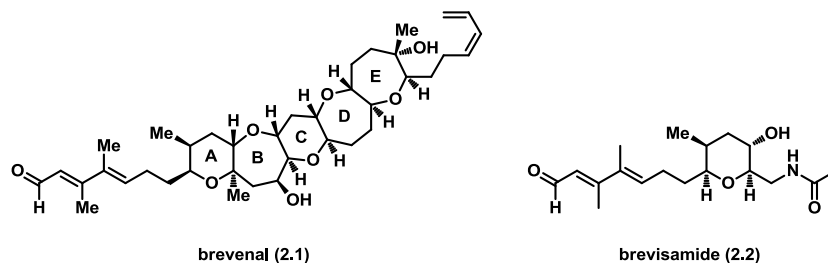
2-1 Introduction

The art and science of natural product total synthesis has become increasingly more associated with the various principles of the “economies” of synthesis.^{32,33} Evaluation of protecting group use serves as one metric of synthetic efficiency and can provide a framework for developing a synthesis plan. Among various classes of natural products prepared by total synthesis without the use of protecting groups, examples featuring polyketides or cyclic ethers are scarce.^{5,34} Herein, we report a concise, enantioselective, protecting-group-free total synthesis of the diversely functionalized cyclic ether natural product brevisamide.

2-2 Brevisamide Background

The “Red Tide” off of the Florida coast and in the Gulf of Mexico has led to the death of a wide range of marine life and human food poisoning.³⁵ Dinoflagellates blooms have been the root cause of this due to the secretion of brevetoxins by *Ptychodiscu brevis*.³⁶ Another species of dinoflagellates, *Karenia brevis* produces the metabolite, brevenal (**2.1**) (Figure 2.2.1), which has been shown to have antagonistic activity against the brevetoxins.³⁷ In 2008, Wright and co-workers isolated another metabolite, brevisamide (**2.2**), from *K. brevis*. This monocyclic ether contains very similar structural features to the A-ring and dienal fragment of brevenal.³⁸

Figure 2.2.1. Brevenal **2.1** and Brevisamide **2.2**



Brevisamide appears to be an important biosynthetic precursor to brevenal and possibly other polycyclic ethers. Brevisamide is comprised of a complex functionalized tetrahydropyran core containing a conjugated 3,4-dimethylhepta-2,4-dienal and acetylated terminal amine subunits. The tetrahydropyran ring also contains methyl and hydroxyl substituents. Since brevisamide has been reported as a biosynthetic precursor to brevenal, a great deal of interest has been generated towards its total synthesis. Multiple groups have synthesized brevisamide since its isolation in 2008, with the first four total syntheses being reported in 2009.

2-3 Previous Syntheses

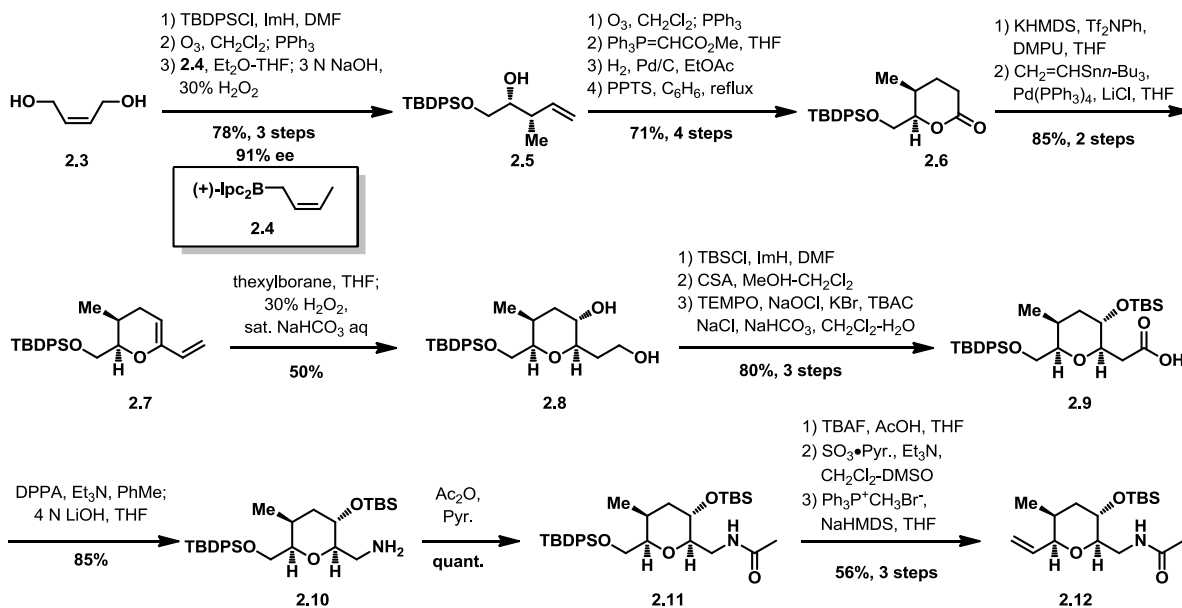
2-3-1 Satake's Synthesis of Brevisamide

The Satake group completed the first total synthesis, outlined in Scheme 2.3.1.³⁹ The tetrahydropyran-core (Scheme 2.3.1, part a) was synthesized by three key reactions: Brown crotylation to generate **2.5**, which led to lactone formation yielding **2.6**, and finally hydroboration was utilized to install the secondary alcohol **2.8**.^{40,41,42} Curtius rearrangement generated primary amine **2.10**, a precursor to amide **2.11**.⁴³ Suzuki-Miyaura cross coupling (part c) of **2.12** and **2.16** installed the diene fragment, which was then followed by MnO₂ oxidation, which completed the first total synthesis of brevisamide (**2.2**) in 21 steps and a

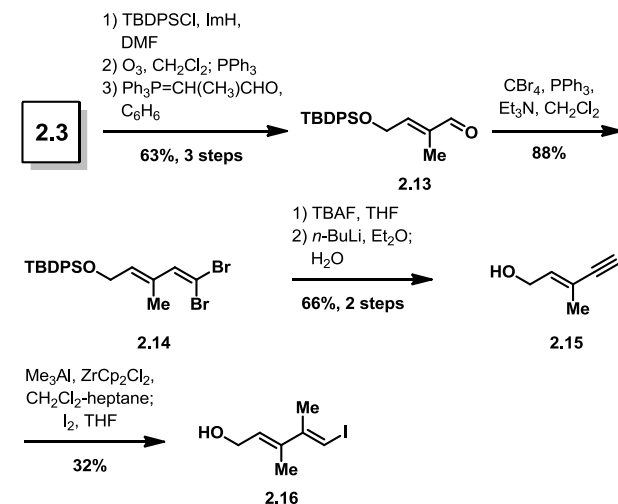
2.0% overall yield. This synthesis also confirmed the absolute stereochemical structure of brevisamide (**2.2**).

Scheme 2.3.1. Satake's Synthesis of Brevisamide **2.2**

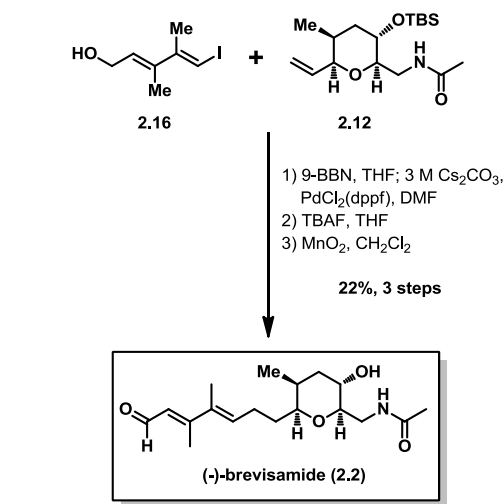
(a) Synthesis of Tetrahydropyran-core



(b) Synthesis of Diene Fragment



(c) Completion of Total Synthesis



2-3-2 Lindsley's Synthesis of Brevisamide

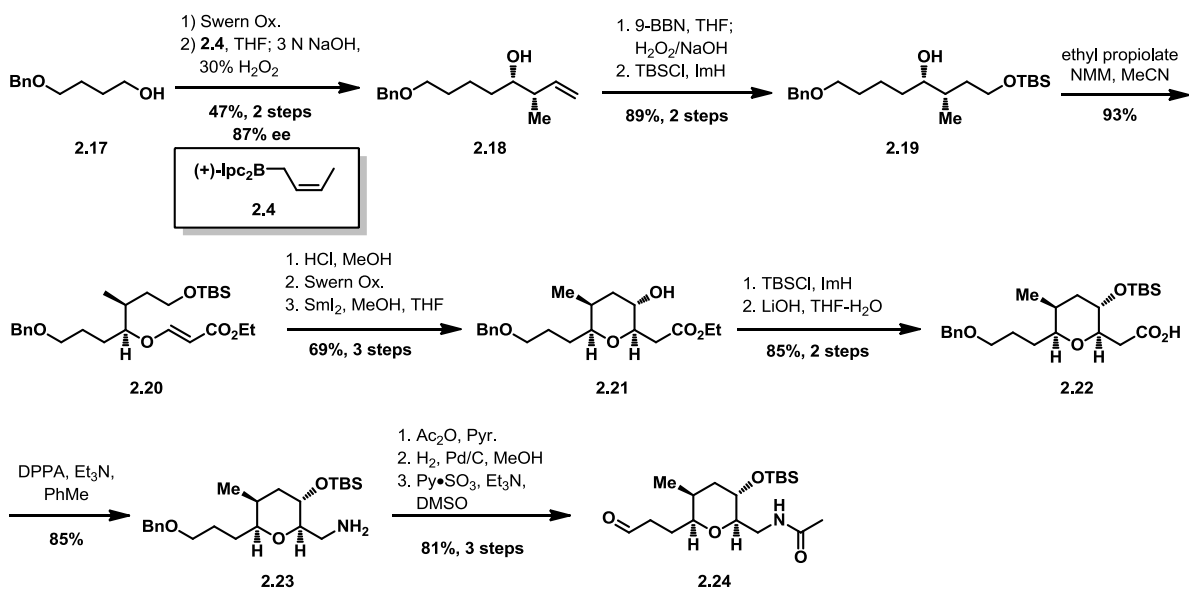
Shortly after the achievement of the first total synthesis, Lindsley and Fadeyi completed another total synthesis.⁴⁴ While their approach was similar to Satake's synthesis in the stepwise construction of the tetrahydropyran-core, they differed in the dienal construction. The tetrahydropyran-core (Scheme 2.3.2, part a) was synthesized by two key reactions: Brown crotylation to generate **2.18** and a samarium(II) iodide reductive cyclization reaction to create the key core **2.21**.⁴⁵ Curtius rearrangement was used to generate the primary amine **2.23** that led to amide **2.24**.⁴⁶ A Horner-Wadsworth-Emmons reaction (part c) of aldehyde **2.24** and phosphonate **2.27** installed the diene fragment, which was then followed by MnO₂ oxidation, which completed the shortest total synthesis of brevisamide (**2.2**) in 18 steps and 6.3% overall yield.

2-3-3 Ghosh's Synthesis of Brevisamide

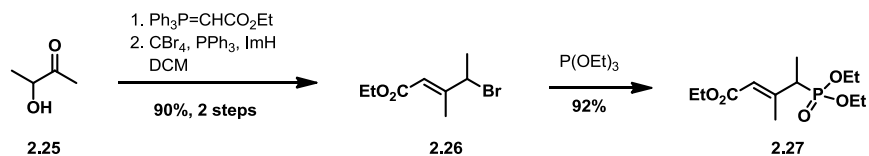
Ghosh and Li completed the third total synthesis.⁴⁷ Their synthesis had an alternative synthetic plan in construction of the tetrahydropyran-core from previous groups. They used Jacobsen's asymmetric Hetero-Diels-Alder reaction of diene **2.31** and aldehyde **2.32** using Jacobsen's chromium catalyst **2.33** to produce **2.34** (Scheme 2.3.3, part a) in high diastereo- and enantioselectivity.⁴⁸ A Rubottom oxidation was used to install the secondary alcohol **2.35**.⁴⁹ Amide **2.38** was produced from a Mitsunobu reaction followed by azide reduction and amine acylation.⁵⁰ A Suzuki-Miyaura cross coupling (part c) of **2.39** and **2.44** installed the diene fragment, which was then followed by TEMPO oxidation that delivered brevisamide (**2.2**) in 19 steps and 1.5% overall yield.⁵¹

Scheme 2.3.2 Lindsley's Synthesis of Brevisamide 2.2

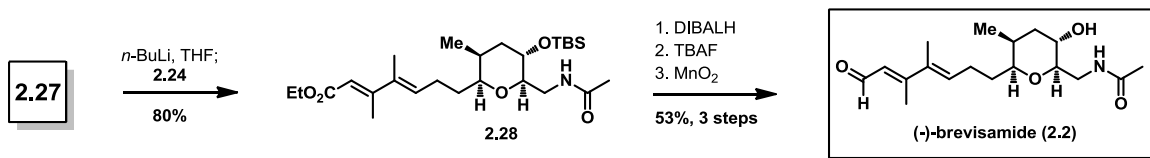
(a) Synthesis of Tetrahydropyran-core



(b) Synthesis of Phosphonate Fragment

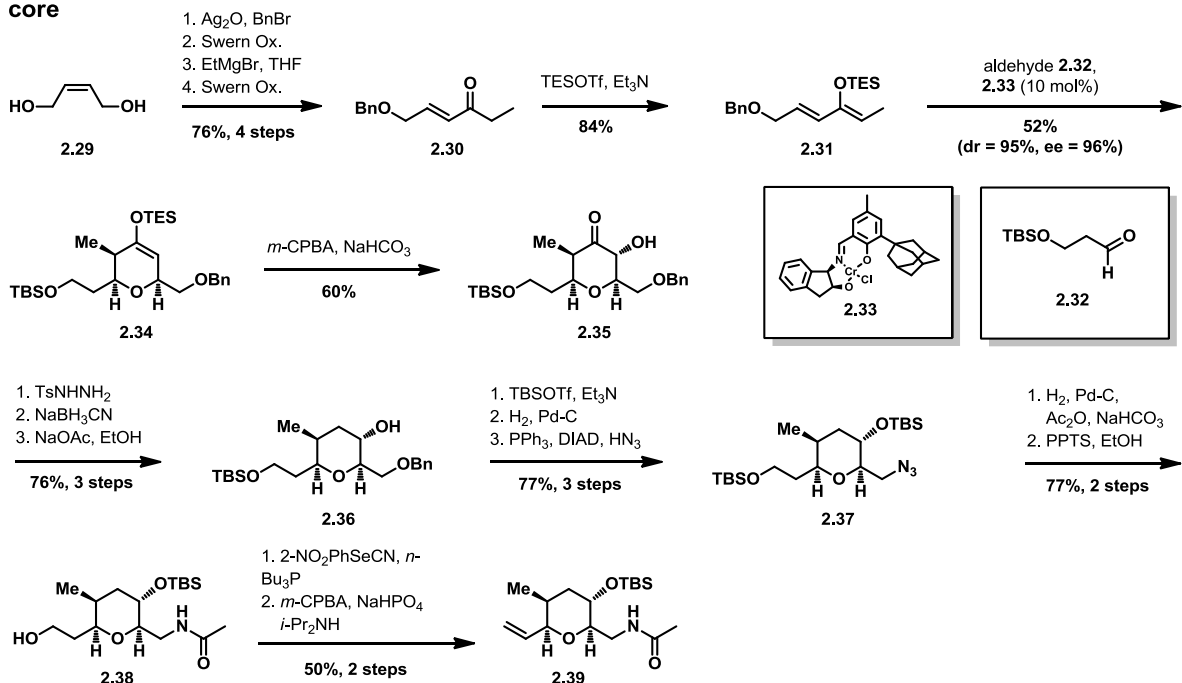


(c) Completion of Total Synthesis

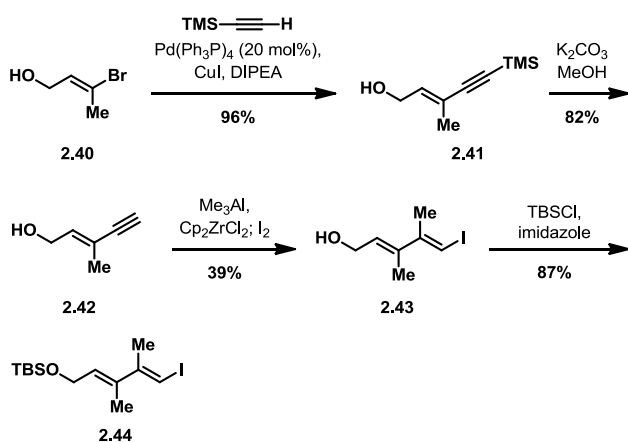


Scheme 2.3.3 Ghosh's Synthesis of Brevisamide 2.2

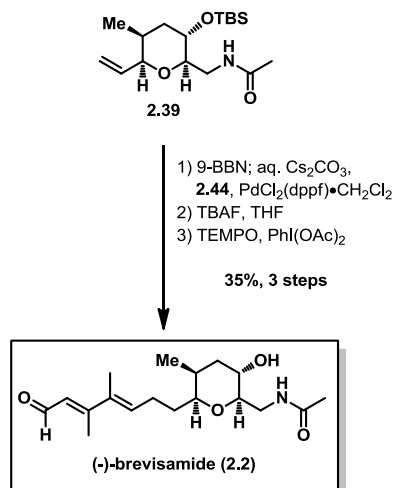
(a) Synthesis of Tetrahydropyran-core



(b) Synthesis of Diene Fragment



(c) Completion of Total Synthesis



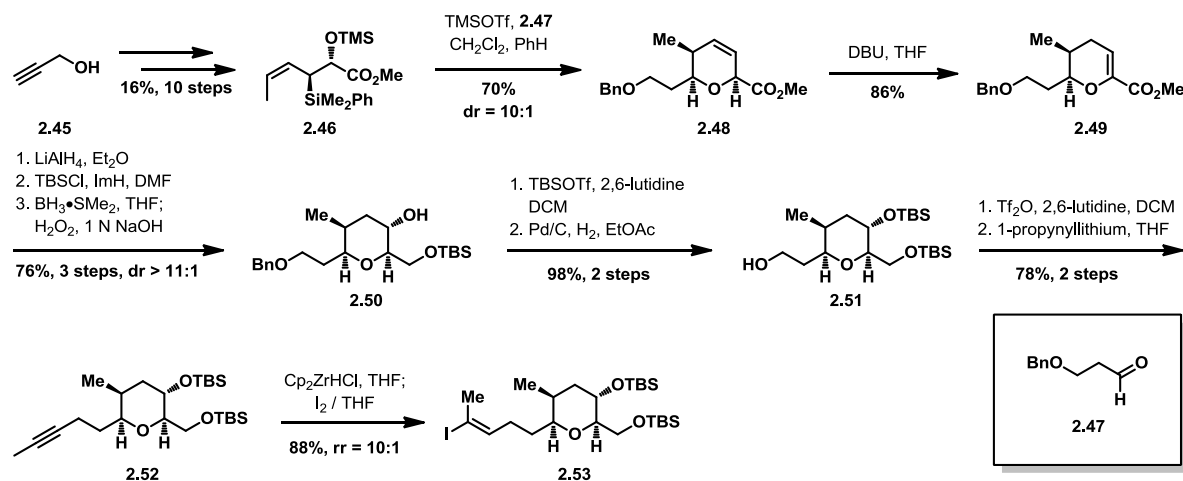
2-3-4 Panek's Synthesis of Brevisamide

Panek and Lee completed the fourth total synthesis of brevisamide (2.2).⁵² Their synthesis centered on Panek's silicon directed [4+2]-annulation utilizing a Z-crotylsilane to construct the tetrahydropyran-core 2.48 (Scheme 2.3.4, part a).⁵³ Hydroboration was used to

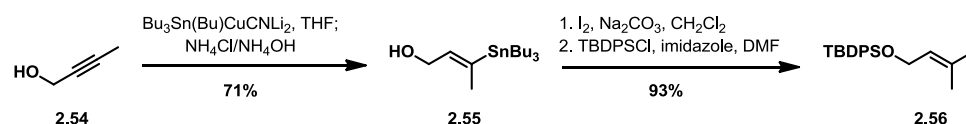
synthesize the equatorial secondary alcohol **2.50**. A Negishi cross-coupling (part c) of **2.53** and **2.56** installed the diene fragment.⁵⁴ The amide **2.58** was produced from a Mitsunobu reaction followed by azide reduction and amine acylation, which was then followed by MnO₂ oxidation, which constructed brevisamide (**2.2**) in 27 steps and 0.8% overall yield.^{55,56}

Scheme 2.3.4 Panek's Synthesis of Brevisamide **2.2**

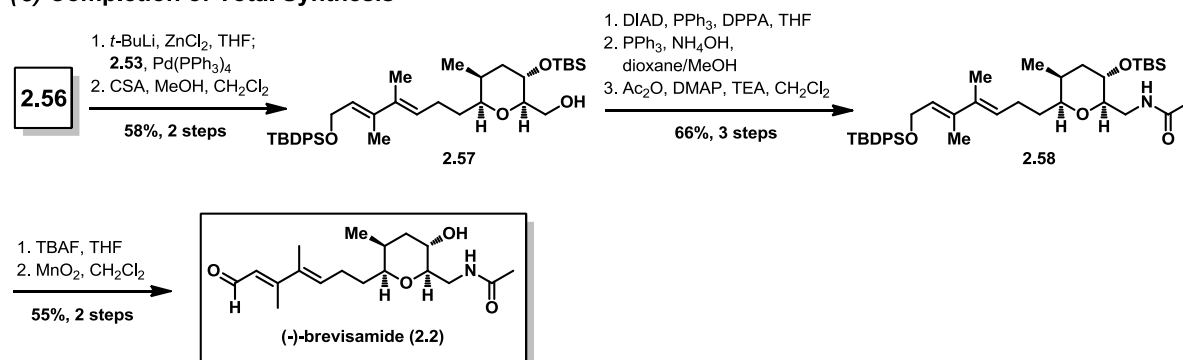
(a) Synthesis of Tetrahydropyran-core



(b) Synthesis of Phosphonate Fragment



(c) Completion of Total Synthesis



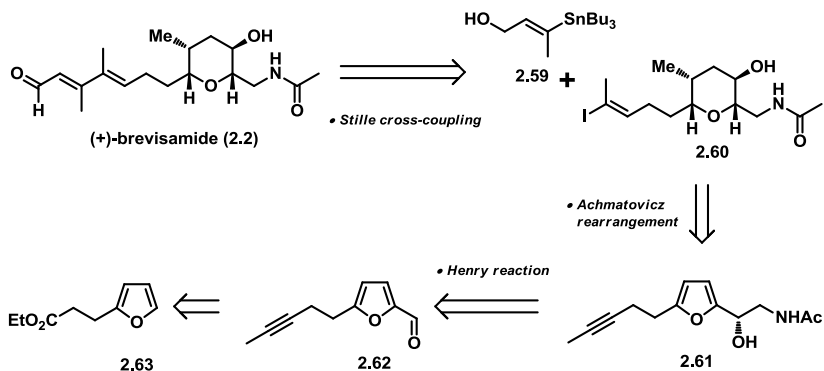
2-3-5 Formal syntheses

Since this latest completed total synthesis, two formal syntheses have been accomplished by the groups of Smith and Sabitha.⁵⁷

2-4 Synthetic Plan of Brevisamide

In devising our own approach, we became intrigued by the challenge of developing a concise, enantioselective, and protecting-group-free construction of the diversely functionalized tetrahydropyran ring in brevisamide. A synthesis plan based on the combination of a catalytic asymmetric Henry reaction and an Achmatowicz rearrangement,⁵⁸ outlined in Scheme 1, proved to be successful in meeting this challenge. The final operation in the synthesis was envisioned to employ a Stille-cross-coupling reaction to install the conjugated (*E,E*)-dieneal.

Scheme 2.4.1 Synthetic Plan of Brevisamide 2.2

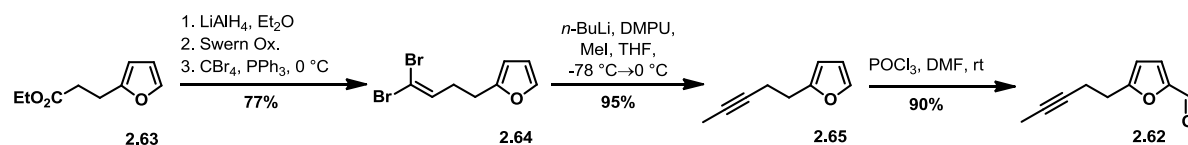


2-5 Total Synthesis of Brevisamide

The synthesis of the aldehyde **2.62**, shown in Scheme 2.5.1, began from commercially available ethyl 3-(furan-2-yl)propionate **2.63**, which was treated with LiAlH_4 to afford the corresponding primary alcohol. After oxidation, the resultant aldehyde was immediately submitted to the Corey–Fuchs reaction yielding dibromoalkene **2.64**,⁵⁹ which was treated

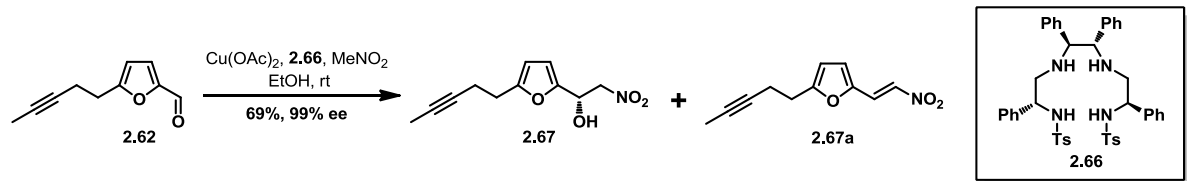
with *n*-butyllithium and iodomethane to form the desired alkyne **2.65**, along with a furan methylation byproduct. Addition of DMPU prior to the addition of iodomethane resulted in the isolation of only the desired methylated alkyne **2.65** in high yield. Aldehyde **2.62** was prepared directly from **2.65** by a Vilsmeier–Haack reaction in 90% yield.⁶⁰

Scheme 2.5.1 Synthesis of Aldehyde **2.62**



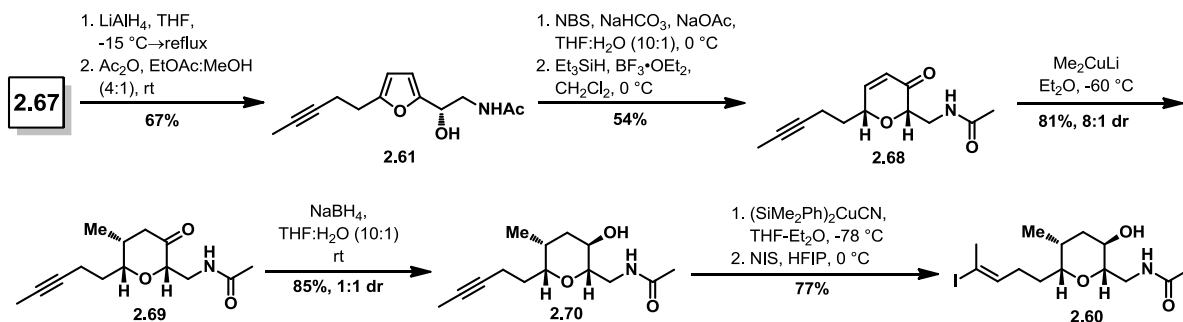
With aldehyde **2.62** in hand, the key enantioselective Henry reaction was investigated. Although a variety of methods are available for this transformation, we focused on a procedure developed by Wan and co-workers.⁶¹ This method has been reported to provide products in high enantioselectivity, under practical reaction conditions at room temperature and within reasonable reaction times. The method employs a catalytic system derived from readily available $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ and ligand **2.66** in ethanol as the solvent. Much to our delight, when **2.62** was exposed to these conditions, the product **2.67** was isolated with a 99% ee. Extended reaction times resulted in accumulation of the nitroalkene **2.67a** as a byproduct resulting from dehydration of the initially formed nitro-alcohol **2.67** (Scheme 2.5.2). To minimize this problem, the reaction was terminated after 40 h at room temperature and the products were separated to provide the requisite Henry addition product **2.67** (57% yield, 99% ee), the starting material (33% yield), and the nitroalkene **2.67a** (10% yield). The starting material was then resubmitted to the reaction conditions to afford **2.67** in a 69% combined yield and 99% ee after one recycle.

Scheme 2.5.2 Asymmetric Henry Reaction



After the development of the enantioselective Henry reaction, the synthesis was advanced as illustrated in Scheme 2.5.3. The nitro group in **2.67** was reduced to the corresponding amine with LiAlH_4 under carefully controlled reaction conditions. Lithium aluminum hydride was preferred to other commonly used reagents for reduction of nitro compounds such as H_2 and Pd/C , Raney-Nickel, and SmI_2 , due to incompatibility of these reagents with the alkyne group present in the substrate.^{33,62} After assessment of a variety of reaction conditions, it was determined that a dropwise addition of a solution of the nitro compound **4** into a precooled solution of LiAlH_4 in THF ($-15\text{ }^\circ\text{C}$) limited the retro-Henry process leading to the formation of an undesired primary alcohol. The reaction was then heated to reflux, which delivered the primary amine in optimized yields. The primary amine was then chemoselectively acetylated with acetic anhydride in ethyl acetate–methanol (4:1), giving amide **2.61** in 67% yield over the two steps.

Scheme 2.5.3 Synthesis of the Tetrahydropyran Core



According to our synthesis plan, acetamide **2.61** was now properly functionalized for the ensuing key Achmatowicz rearrangement. Furan **2.61** underwent oxidative ring expansion in the presence of NBS to form the cyclic hemiketal, which was then treated with $\text{BF}_3 \cdot \text{OEt}_2$ and Et_3SiH to produce intermediate **2.68** in a satisfactory 54% yield.⁶³ Installation of the methyl group was achieved by conjugate addition of lithium dimethylcuprate directly to enone **2.68** (81% yield, 8:1 dr).⁶⁴

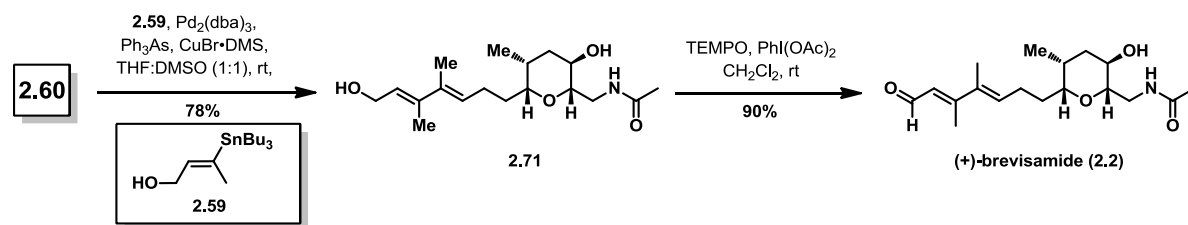
Our next goal was reduction of **2.69** under thermodynamic conditions to generate the more stable diastereomer **2.70** that has the desired configuration at the newly generated stereocenter. Our initial attempts centered on various versions of the Meerwein–Ponndorf–Verley (MPV) reaction using $\text{Al}(\text{OPr-}i)_3$ and $\text{Sm}(\text{OPr-}i)_3$ reagents. With the aluminum-based reagent, the desired diastereomer **2.70** was formed exclusively at high temperatures (100 °C), however, at low yields. An unidentified byproduct was formed in significant quantities apparently resulting from reactivity of the acetamide. At lower temperatures (75 °C), an equimolar mixture of diastereomeric alcohols was produced. A ligand-based reduction was used in our next approach, employing (*R*)-CBS catalyst. This method led to a mixture of diastereomeric alcohols, with poor selection. Similar outcomes were observed with the samarium-based reagent. Reduction with sodium borohydride under standard conditions in methanol produced the undesired axial alcohol exclusively. On the other hand, reduction with NaBH_4 in aqueous THF substantially increased the fraction of the desired equatorial alcohol, giving a 1:1 mixture of separable products in 85% isolated yield.⁶⁵ The undesired isomer could be separated and recycled through an additional oxidation–reduction sequence.

Installation of vinyl iodide proceeded in high regioselectivity and yield employing the silylcupration-iododesilylation protocol.^{66,67} Silylcupration took place with complete stereoselectivity and high regioselectivity (~13:1). Subsequent iododesilylation with *N*-

iodosuccinimide (NIS) in hexafluoroisopropanol (HFIP) successfully delivered the (*E*)-iodoalkene **2.60** in high yield and with complete retention of the double bond geometry.^{38,68}

Known vinyltin reagent **2.59** (prepared by hydrostannylation of 2-butyne-1-ol)⁶⁹ was used in a Stille cross-coupling reaction with **2.60** to forge the conjugated diene (Scheme 2.5.4). Sasaki and co-workers previously reported a similar Stille coupling in the total synthesis of brevenal.³⁹ In our work, copper(I) thiophene-2-carboxylate was replaced with the copper(I) bromide dimethylsulfide complex (CuBr•DMS) without any detrimental effect on the Pd₂(dba)₃/Ph₃As-catalyzed cross-coupling process, furnishing **2.71** in 78% yield. Completion of the synthesis was achieved with a chemoselective oxidation of the allylic alcohol using TEMPO in the presence of PhI(OAc)₂ in CH₂Cl₂ at room temperature, yielding (+)-brevisamide (**2.2**) in 90% yield.¹⁹

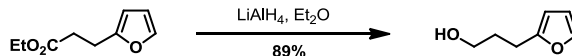
Scheme 2.5.4 Completion of Brevisamide (**2.2**) Synthesis



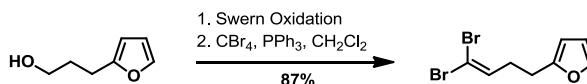
2-6 Conclusion

In summary, the total synthesis of (+)-brevisamide (**2.2**) has been completed in 16 steps (longest linear sequence) and an overall yield of 2.5% starting from the commercially available ethyl 3-(furan-2-yl)propionate **2.63**. The strategy was developed based on a notion of concise enantioselective assembly of the properly functionalized tetrahydropyran ring without the use of protecting groups. A catalytic asymmetric Henry reaction and then an Achmatowicz rearrangement were enlisted to successfully achieve this goal.

2-7: Brevisamide Supporting Information



3-(Furan-2-yl)propan-1-ol (2.72). Lithium aluminum hydride (4.29 g, 113 mmol, 3.0 equiv.) in diethyl ether (160 mL) was cooled to $-78\text{ }^\circ\text{C}$. Ethyl 3-(furan-2-yl)propionate (**2.63**) (6.00 mL, 37.6 mmol) in diethyl ether (28 mL total with rinses) was added to the reaction vessel. After 10 min of stirring at $-78\text{ }^\circ\text{C}$, the reaction vessel was allowed to warm to $0\text{ }^\circ\text{C}$ and was stirred for 1 h. The reaction vessel was then warmed to rt and stirred for an additional 1 h before cooling back to $0\text{ }^\circ\text{C}$ and slowly quenching with diH_2O (4.29 mL). The reaction mixture was stirred for 5 min at $0\text{ }^\circ\text{C}$ at which time a 15 wt% NaOH (4.29 mL) solution and diH_2O (12.9 mL) were added sequentially and stirred for 5 min. The reaction vessel was then warmed to rt and stirred until a white precipitate and a clear organic solution were formed. The precipitate was filtered off and washed with diethyl ether, and the organic solution was collected and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 30% ethyl acetate – hexanes) delivering product **2.72** (4.21 g, 33.4 mmol, 89%). ^1H NMR (400 MHz, CDCl_3); $\delta(\text{ppm})$: 7.31-7.30 (m, 1H); 6.28 (dd, $J_1=3.2\text{ Hz}$, $J_2=2.0\text{ Hz}$, 1H); 6.01 (dd, $J_1=3.2\text{ Hz}$, $J_2=1.2\text{ Hz}$, 1H); 3.69 (dd, $J_1=J_2=6.0\text{ Hz}$, 2H); 2.74 (dd, $J_1=J_2=7.2\text{ Hz}$, 2H); 1.95-1.86 (m, 2H); 1.42 (br s, 1H).⁷⁰

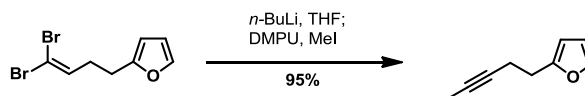


2-(4,4-Dibromobut-3-en-1-yl)furan (2.64). Dimethylsulfoxide (1.70 mL, 24.1 mmol, 3.0 equiv.) was added to oxalyl chloride (1.05 mL, 12.0 mmol, 1.5 equiv.) in dichloromethane (30 mL) at $-78\text{ }^\circ\text{C}$ and was stirred for 15 min. Substrate **2.72** (1.00 g, 7.93 mmol) in

dichloromethane (22.8 mL total with rinses) was transferred to the reaction vessel and stirred at -78 °C for 25 min. Triethylamine (5.00 mL, 35.9 mmol, 4.5 equiv.) was added to the reaction vessel and stirred for 10 min at -78 °C. The solution was then warmed to rt and stirred for an additional 10 min before 1.0 M HCl (30 mL); diH₂O (30 mL); diethyl ether (75 mL) were added. The phases were separated, and the aqueous phase was extracted with diethyl ether (3x50 mL). The combined organic phases were washed with a 1:1 v/v mixture of brine and saturated aqueous sodium bicarbonate and dried over sodium sulfate. The volatile crude aldehyde was concentrated by simple distillation at 60 °C to a volume of 5-10 mL remained at which point pentane (20 mL) was added and the distillation was continued until 5-10 mL remained. The crude organic mixture was then purified rapidly by column chromatography (silica, 30% diethyl ether – pentane) to avoid the decomposition of the aldehyde. Fractions containing the aldehyde were collected and concentrated by simple distillation at 60 °C until 5-10 mL remained, which was submitted to the Corey-Fuchs reaction.

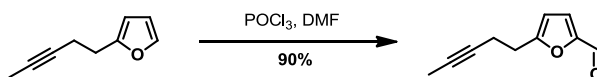
Triphenylphosphine (8.32 g, 31.7 mmol, 4.0 equiv.) was added to a solution of carbon tetrabromide (5.27 g, 15.9 mmol, 2.0 equiv.) in dichloromethane (15.4 mL) at 0 °C and stirred for 30 min. Then the diluted pure aldehyde (*ca.* 7.93 mmol) in dichloromethane (10.0 mL total with rinses) was added to the reaction vessel and stirred for 15 min at 0 °C. The reaction mixture was quenched with the addition of diH₂O (20 mL) and diethyl ether (40 mL). The phases were separated, and the aqueous layer was extracted with diethyl ether (3x20 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*. Removal of the triphenylphosphine oxide was accomplished by addition of a small amount of diethyl ether (5 mL) to the crude product

followed by addition of pentane (60 mL) with agitation, which caused formation of a white solid (triphenylphosphine oxide). Solids were filtered through a plug column and washed with pentane. The collected organic phase was concentrated *in vacuo*. The residue was purified by column chromatography (silica, 100% pentane) delivering product **2.64** (1.93 g, 6.90 mmol, 87% over 2 steps). ¹H NMR (400 MHz, CDCl₃); δ(ppm): 7.33-7.31 (m, 1H); 6.42 (dd, *J*₁=3.2, *J*₂=2.0 Hz, 1H); 6.29 (dd, *J*₁=3.2 Hz, *J*₂=2.0 Hz, 1H); 6.03 (dd, *J*₁=3.2 Hz, *J*₂=0.8 Hz, 1H); 2.76 (dd, *J*₁=*J*₂=7.2 Hz, 2H); 2.44 (ddd, *J*₁=*J*₂=*J*₃=7.2 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 154.3, 141.5, 137.4, 110.4, 105.8, 90.0, 31.8, 26.4. LRMS (ESI) calcd for C₈H₉Br₂O [M+H] 278.90, found 279.89.



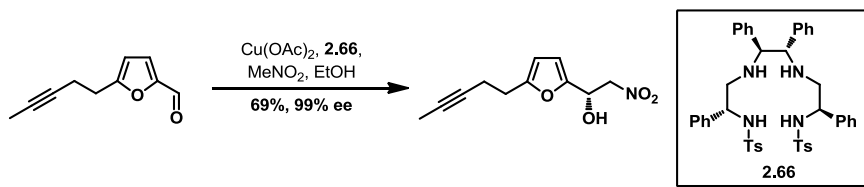
2-(Pent-3-yn-1-yl)furan (2.65). Substrate **2.64** (0.240 g, 0.857 mmol) in THF (1.10 mL) was cooled to -78 °C. *n*-Butyllithium (2.47 M, 1.05 mL, 2.59 mmol, 3.0 equiv.) was added to the reaction mixture and stirred for 1.25 h at -78 °C. DMPU (0.310 mL, 2.56 mmol, 3.0 equiv.) was added to the mixture at -78 °C and stirred for 5 min; followed by addition of methyl iodide (1.00 mL, 16.1 mmol, 18.8 equiv.). The reaction mixture was stirred for 1 h at -78°C and was then warmed to rt and stirred for an additional 1 h before adding saturated aqueous ammonium chloride. The resulting phases were separated, and the aqueous phase was extracted with diethyl ether (3x5 mL). The combined organic phases were washed with diH₂O (3x10 mL); brine (2x10 mL); dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 100% pentane) delivering product **2.65** (0.1094 g, 0.815 mmol, 95%). ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.31-7.30

(m, 1H); 6.29-6.28 (m, 1H); 6.07-6.05 (m, 1H); 2.82 (dd, $J_1=J_2=7.0$ Hz, 2H); 2.48–2.43 (m, 2H); 1.77 (dd, $J_1=J_2=2.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 154.8, 141.2, 110.3, 105.5, 78.2, 76.4, 28.2, 18.2, 3.8. LRMS (ESI) calcd for $\text{C}_9\text{H}_{10}\text{O}$ [M] 134.07, found 134.07.



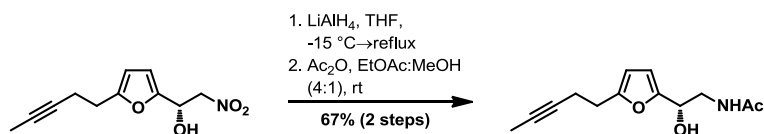
5-(Pent-3-yn-1-yl)furan-2-carbaldehyde (2.62). Dimethylformamide (1.35 mL, 17.4 mmol, 1.3 equiv.) was added to pre-cooled (0 °C) phosphonyl trichloride (1.35 mL, 14.7 mmol, 1.1 equiv.). The reaction vessel was capped and heated to 85 °C for 1.5 h. The reaction vessel was then cooled to 0 °C and substrate **8** (1.77 g, 13.2 mmol) in dimethylformamide (6.60 mL total with rinses) was added and stirred for 5 min. The reaction vessel was then capped, warmed to rt, and stirred for 24 h. The reaction mixture was added slowly to saturated aqueous sodium bicarbonate (50 mL) to quench the reaction. Additional saturated aqueous sodium bicarbonate was added until the reaction mixture had a pH 8-9. The phases were separated and the aqueous phase was extracted with dichloromethane (3x20 mL). The combined organic phases were then washed with a 1:1 mixture of brine and saturated aqueous sodium bicarbonate, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 20% ethyl acetate - hexane) delivering product **2.62** (1.93 g, 11.9 mmol, 90%). ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 9.54 (s, 1H); 7.18 (d, $J=4.0$ Hz, 1H); 6.34 (d, $J=4.0$ Hz, 1H); 2.91 (dd, $J_1=J_2=7.5$ Hz, 2H); 2.55–2.50 (m, 2H); 1.75 (dd, $J_1=J_2=2.5$ Hz, 3H). ^{13}C NMR (125

MHz, C₆D₆); δ (ppm): 176.8, 161.4, 153.0, 121.8, 109.3, 77.8, 77.3, 28.6, 18.0, 3.7. LRMS (ESI) calcd for C₁₀H₁₀O₂ [M] 162.07, found 162.07.



(S)-2-Nitro-1-(5-(pent-3-yn-1-yl)furan-2-yl)ethanol (2.67). Copper(II) acetate monohydrate (30.9 mg, 0.155 mmol, 0.025 equiv.) and ligand **2.66**⁷¹ (0.235 g, 0.310 mmol, 0.050 equiv.) were dissolved in freshly distilled ethanol (6.20 mL) and stirred at rt for 1 h. Substrate **2.62** (1.00 g, 6.17 mmol) in freshly distilled ethanol (6.20 mL total with rinses) was added to the reaction vessel, followed by addition of freshly distilled nitromethane (6.60 mL, 123 mmol, 20 equiv.) and stirred at rt for 40 h. The reaction mixture was concentrated *in vacuo* and the residue was purified rapidly by column chromatography (silica, 10% diethyl ether – pentane, 30 % diethyl ether – pentane). The recovered starting material was then resubmitted to similar reaction conditions. Copper(II) acetate monohydrate (9.4 mg, 47 μ mol, 0.025 equiv.) and ligand **2.66** (71.3 mg, 94 μ mol, 0.050 equiv.) were dissolved in freshly distilled ethanol (1.90 mL) and stirred at rt for 1 h. Recovered substrate **2.62** (0.304 g, 1.87 mmol) in freshly distilled ethanol (1.90 mL total with rinses) was added to the reaction vessel, followed by addition of freshly distilled nitromethane (2.00 mL, 37.4 mmol, 20 equiv.) and stirred at rt for 72 h. The reaction mixture was concentrated *in vacuo* and the residue was purified rapidly by column chromatography (silica, 10% diethyl ether – pentane, 30 % diethyl ether – pentane) delivering the combined product **2.67** (0.955 g, 4.28 mmol, 69%); ee >99% by chiral HPLC analysis (Daicel Chiralcel OJ-H, 10% *i*-PrOH/hexanes,

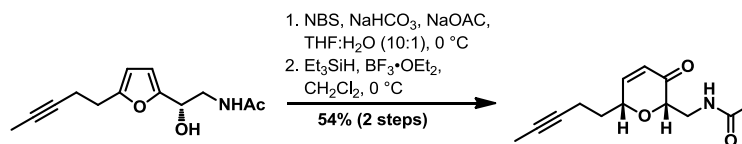
$\lambda=215$ nm, $r=1.0$ ml/min, $R_t=30.6$ min). $[\alpha]_D^{23}$ -38.6 (c 10.0, CHCl_3). ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 6.29 (d, $J1=4.0$ Hz, 1H); 6.06 (d, $J1=4.0$ Hz, 1H); 5.45-5.40 (m, 1H); 4.78 (dd, $J1=14.0$ Hz, $J2=9.5$ Hz, 1H); 4.66 (dd, $J1=14.0$ Hz, $J2=3.5$ Hz, 1H); 2.79 (dd, $J1=J2=7.0$ Hz, 2H); 2.66 (d, $J1=5.5$ Hz, 2H); 2.47–2.41 (m, 2H); 1.77 (dd, $J1=J2=2.5$ Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD); $\delta(\text{ppm})$: 156.6, 152.3, 109.3, 107.5, 80.2, 78.7, 77.1, 65.9, 29.1, 18.7, 3.2. LRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_4\text{Na}$ $[\text{M}+\text{Na}]$ 246.07, found 246.09.



(S)-N-(2-Hydroxy-2-(5-(pent-3-yn-1-yl)furan-2-yl)ethyl)acetamide (2.61). Lithium aluminum hydride (0.681 g, 17.9 mmol, 3.0 equiv.) in THF (18.0 mL) was cooled to $-15\text{ }^\circ\text{C}$. Substrate **2.67** (0.802 g, 3.59 mmol) in THF (54 mL total with rinses) was slowly added to the reaction vessel and stirred for 30 min at $-15\text{ }^\circ\text{C}$. The reaction mixture was warmed to rt and stirred for 30 min; then heated to reflux for 1.5 h before cooling back to $0\text{ }^\circ\text{C}$ and slowly quenching with diH_2O (0.68 mL). The reaction mixture was stirred for 5 min at the same temperature at which time 15 wt% NaOH (0.68 mL) and diH_2O (2.05 mL) were added sequentially and stirred for 5 min. The reaction mixture was warmed to rt and stirred for 4 hours (until an off-white precipitate formed). The precipitate was filtered off and washed with diethyl ether. The collected organic phase was concentrated *in vacuo* and submitted to the next reaction without further purification.

The crude substrate was suspended in ethyl acetate (11.5 mL) and methanol (2.90 mL). Acetic anhydride (0.370 mL, 3.91 mmol, 1.1 equiv.) was added to the reaction vessel and

stirred at rt for 12 h. An aqueous solution of 10 wt% K₂CO₃ (15 mL) was added to the reaction vessel and stirred at rt for 10 min. The resulting phases were separated and the aqueous phase was extracted with ethyl acetate (3x10 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 80% ethyl acetate – hexanes, 90% ethyl acetate – hexanes, 100% ethyl acetate – hexanes, 95% ethyl acetate – methanol) delivering product **2.61** (0.567 g, 2.41 mmol, 67% over 2 steps). $[\alpha]_D^{23}$ -35.4 (c 10.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃); δ(ppm): 6.19 (d, *J*₁=3.0 Hz, 1H); 6.01 (d, *J*₁=3.0 Hz, 1H); 5.96 (br s, 1H); 4.79-4.75 (m, 1H); 3.75 (ddd, *J*₁=14.0 Hz, *J*₂=6.5 Hz, *J*₃=3.5 Hz, 1H); 3.51 (ddd, *J*₁=13.5 Hz, *J*₂=7.5 Hz, *J*₃=5.5 Hz, 1H); 3.12-3.10 (m, 1H); 2.78 (dd, *J*₁=*J*₂=7.0 Hz, 2H); 2.46–2.41 (m, 2H); 2.01 (s, 3H); 1.77 (dd, *J*₁=*J*₂=2.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 171.6, 154.8, 152.8, 107.7, 106.4, 78.1, 76.6, 67.7, 44.6, 28.1, 23.4, 18.1, 3.7. LRMS (ESI) calcd for C₁₃H₁₇NO₃Na [M+Na] 258.11, found 258.12.

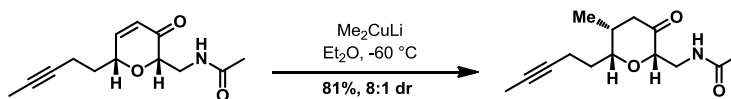


***N*-(((2R,6S)-3-Oxo-6-(pent-3-yn-1-yl)-3,6-dihydro-2H-pyran-2-yl)methyl)acetamide**

(2.68). *N*-bromo-succinimide (0.223 g, 1.25 mmol, 1.0 equiv.) was added to a mixture of substrate **2.61** (0.293 g, 1.25 mmol), sodium bicarbonate (0.210 g, 2.50 mmol, 2.0 equiv.), and sodium acetate (0.103 g, 1.25 mmol, 1.0 equiv.) in THF (7.90 mL) and diH₂O (2.6 mL) at 0 °C (the reaction vessel was open to air). The reaction vessel was stirred at 0 °C for 1.5 h before addition of saturated aqueous ammonium chloride (10 mL). The phases were

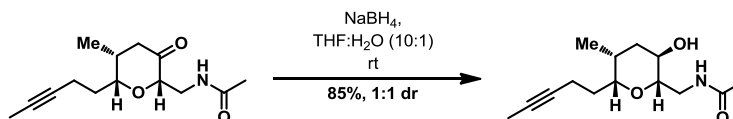
separated and the aqueous phase was extracted with ethyl acetate (3x10 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*. The crude product was submitted to the next reaction without further purification.

The crude substrate in dichloromethane (12.5 mL) was cooled to 0 °C. Triethylsilane (1.00 mL, 6.26 mmol, 5.0 equiv.) was added to the reaction vessel followed by addition of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (0.310 mL, 2.51 mmol, 2.0 equiv.) at 0 °C and stirring for 30 min. The reaction was quenched by addition of saturated aqueous sodium bicarbonate (15 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3x10 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 80% ethyl acetate – hexanes) delivering product **2.68** (0.159 g, 0.676 mmol, 54% over 2 steps). $[\alpha]_{\text{D}}^{23}$ 22.5 (*c* 10.0, CHCl_3). ^1H NMR (400 MHz, CDCl_3); $\delta(\text{ppm})$: 6.95 (dd, $J_1=10.4$ Hz, $J_2=1.6$ Hz, 1H); 6.09 (dd, $J_1=10.4$ Hz, $J_2=2.4$ Hz, 1H); 6.02 (br s, 1H); 4.55–4.49 (m, 1H); 4.04 (ddd, $J_1=J_2=5.60$ Hz, $J_3=1.6$ Hz, 1H); 3.70–3.55 (m, 2H); 2.38–2.22 (m, 2H); 1.97 (s, 3H); 1.86–1.79 (m, 2H); 1.76 (dd, $J_1=J_2=2.4$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3); $\delta(\text{ppm})$: 195.9, 170.2, 151.8, 127.0, 78.1, 77.8, 77.0, 73.1, 39.4, 34.0, 23.5, 14.7, 3.7. LRMS (ESI) calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]$ 258.11, found 258.11.

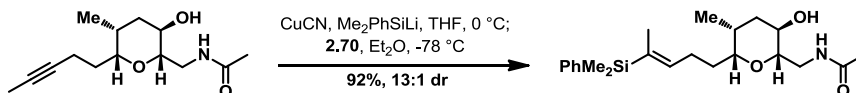


***N*-(((2R,5S,6S)-5-Methyl-3-oxo-6-(pent-3-yn-1-yl)tetrahydro-2H-pyran-2-yl)methyl)acetamide (2.69).** Methyl-lithium (1.64 M in diethyl ether, 1.19 mL, 1.95 mmol,

3.3 equiv.) was added to a solution of copper(I) bromide-dimethyl sulfide complex (0.200 g, 0.973 mmol, 1.65 equiv.) in diethyl ether (1.35 mL) at -60 °C. The reaction vessel was warmed to -30 °C and stirred for 20 min then cooled to -78 °C and substrate **2.68** (0.138 g, 0.587 mmol) in diethyl ether (4.50 mL total with rinses) was added dropwise. The reaction vessel was stirred at -78 °C for 1 h and then warmed to 0 °C over 30 min before being quenched with a 9:1 v/v solution of saturated aqueous ammonium chloride and ammonium hydroxide (15 mL). The biphasic mixture was stirred for 3 h at rt (until a dark blue solution formed). The phases were separated and the aqueous phase was extracted with diethyl ether (3x10 mL). The combined organic phases were washed with brine, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 80% ethyl acetate – hexanes) delivering product **2.69** (0.120 g, 0.477 mmol, 81%, 8:1 dr). A sample of the diastereomers was separated using preparative HPLC. The separation was conducted on a YMC-Pack Sil HPLC column (250x30mmID, S-10 μ m, 12 nm) with 2.0 mL injection (10% *i*-PrOH/hexanes as eluent at a rate of 20 mL/min, λ =210 nm, R_t =48.0 min) afforded pure product **12** (80.4 mg, 0.320 mmol). $[\alpha]_D^{23}$ 52.3 (c 10.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 5.86 (br s, 1H); 4.01 (ddd, J_1 =9.0 Hz, J_2 =4.5 Hz, J_3 =2.0 Hz, 1H); 3.92 (dd, J_1 = J_2 =6.0 Hz, 1H); 3.58 (ddd, J_1 =14.0 Hz, J_2 = J_3 =6.0 Hz, 1H); 3.49 (ddd, J_1 =14.0 Hz, J_2 = J_3 =6.0 Hz, 1H); 2.71 (dd, J_1 =15.0 Hz, J_2 =6.0 Hz, 1H); 2.34 (dd, J_1 =15.0 Hz, J_2 =2.0 Hz, 1H); 2.32–2.25 (m, 3H); 1.97 (s, 3H); 1.80–1.73 (m, 3H); 1.79 (dd, J_1 = J_2 =2.5 Hz, 3H); 1.60–1.54 (m, 1H); 0.94 (d, J_1 =6.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 208.1, 170.1, 80.5, 78.4, 78.0, 76.4, 47.4, 39.1, 36.0, 31.9, 23.6, 15.9, 13.5, 3.8. LRMS (ESI) calcd for C₁₄H₂₁NO₃Na [M+Na] 274.14, found 274.15.

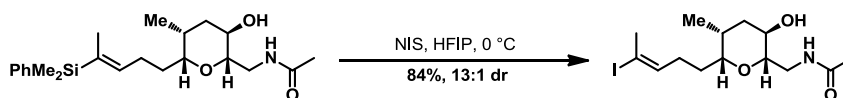


***N*-(((2R,3S,5S,6S)-3-Hydroxy-5-methyl-6-(pent-3-yn-1-yl)tetrahydro-2H-pyran-2-yl)methyl)acetamide (2.70).** Sodium borohydride (21.8 mg, 0.576 mmol, 4.0 equiv.) in diH₂O (0.26 mL) was added dropwise to substrate **2.69** (36.3 mg, 0.144 mmol) in THF (2.60 mL) at rt and stirred for 5 min before it was quenched with saturated aqueous ammonium chloride (5 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (3x5 mL). The combined organic phases were washed with brine, dried over sodium sulfate, concentrated *in vacuo*. The residue was purified by column chromatography (silica, 70% ethyl acetate – hexanes to 100% ethyl acetate - hexanes) delivering product **2.70** (15.5 mg, 61.2 μ mol, 42.5%) as a single diastereomer. $[\alpha]_D^{23}$ 124.5 (c 10.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 5.96 (br s, 1H); 3.99–3.93 (m, 2H); 3.54–3.50 (m, 1H); 3.46–3.40 (m, 1H); 3.14–3.07 (m, 2H); 2.27–2.12 (m, 2H); 2.05 (s, 3H); 1.94 (ddd, *J*₁=12.5 Hz, *J*₂=4.5 Hz, *J*₃=2.5 Hz, 1H); 1.90–1.83 (m, 1H); 1.78 (dd, *J*₁=*J*₂=2.5 Hz, 3H); 1.70–1.59 (m, 2H); 1.50–1.44 (m, 1H); 0.91 (d, *J*₁=7.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 172.3, 82.6, 79.1, 78.8, 76.0, 62.3, 41.2, 38.6, 32.8, 32.4, 23.2, 15.9, 13.1, 3.8. LRMS (ESI) calcd for C₁₄H₂₃NO₃Na [M+Na] 276.33, found 276.19.

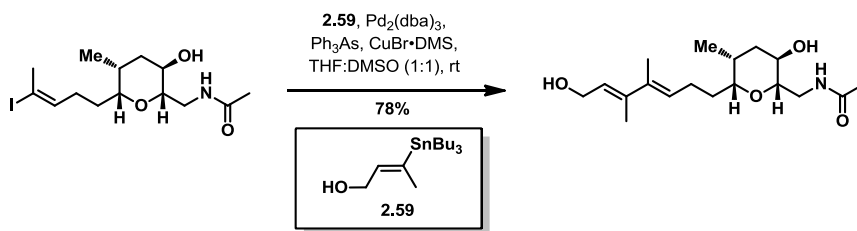


***N*-(((2R,5S,6S)-6-((E)-4-(Dimethyl(phenyl)silyl)pent-3-en-1-yl)-5-methyl-3-oxotetrahydro-2H-pyran-2-yl)methyl)acetamide (2.73).** PhMe₂SiLi (0.9 M solution in

THF, 4.20 mL, 3.78 mmol, 20 equiv.) was added to a solution of copper cyanide (0.170 g, 1.90 mmol, 10 equiv.) in THF (4.80 mL) at 0 °C and stirred for 20 minutes. The reaction vessel was cooled to -78 °C followed by addition of substrate **2.70** (47.9 mg, 0.189 mmol) in ether (6.30 mL total with rinses) and then THF (0.30 mL). The reaction vessel was stirred at -78 °C for 1 h and was warmed to 0 °C and stirred for 1 h before being quenched with a 9:1 v/v solution of saturated aqueous ammonium chloride and ammonium hydroxide (15 mL). The biphasic mixture was stirred for 3 h at rt (until a dark blue aqueous solution formed). The phases were separated and the aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic phases were washed with saturated aqueous sodium bicarbonate, brine, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 60% ethyl acetate – hexanes to 80% ethyl acetate – hexanes) delivering product **2.73** (68.2 mg, 0.175 mmol, 93%,) as a 13:1 inseparable mixture of regioisomers. $[\alpha]_D^{23}$ 62.1 (*c* 5.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.52-7.46 (m, 2H); 7.36-7.32 (m, 3H); 5.97 (br s, 1H); 5.78 (ddd, *J*₁=*J*₂=7.0 Hz, *J*₃=1.5 Hz, 1H); 4.03–3.89 (m, 2H); 3.47–3.34 (m, 2H); 3.12–3.02 (m, 2H); 2.22-2.10 (m, 2H); 2.04 (s, 3H); 1.94 (ddd, *J*₁=13.0 Hz, *J*₂=4.5 Hz, *J*₃=2.5 Hz, 1H); 1.90–1.82 (m, 1H); 1.66 (s, 3H); 1.65–1.51 (m, 2H); 1.41–1.32 (m, 1H); 0.92 (d, *J*₁=6.5 Hz, 3H); 0.32 (s, 6H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 172.3, 141.0, 138.9, 135.0, 134.1, 129.0, 127.9, 82.7, 80.0, 62.2, 41.2, 38.7, 32.8, 32.3, 25.3, 23.2, 14.9, 12.9, -3.2. LRMS (ESI) calcd for C₃₂H₃₅NO₂SiNa [M+Na] 412.23, found 412.23.

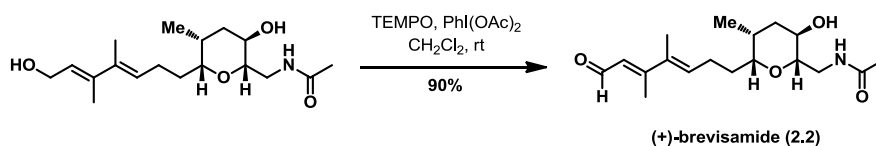


***N*-(((2R,5S,6S)-6-((E)-4-Iodopent-3-en-1-yl)-5-methyl-3-oxotetrahydro-2H-pyran-2-yl)methyl)acetamide (2.60).** *N*-Iodosuccinimide (74.7 mg, 0.332 mmol, 2.0 equiv.) was added to a solution of substrate **2.73** (64.8 mg, 0.166 mmol) and 2,6-lutidine (15.5 μ L, 0.133 mmol, 0.8 equiv.) in hexafluoroisopropanol (1.70 mL) at 0 °C and stirred for 5 min. Ethyl acetate (3 mL) and diH₂O (3 mL) were added to the reaction mixture. The phases were separated and the aqueous phase was extracted with ethyl acetate (3x5 mL). The combined organic phases were washed with saturated aqueous sodium thiosulfate (10 mL); 1 M HCl (10 mL); diH₂O (10 mL); brine, dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 60% ethyl acetate – hexanes to 80% ethyl acetate - hexanes) delivering product **2.60** (53.0 mg, 0.139 mmol, 84%) as a 13:1 inseparable mixture of regioisomers. $[\alpha]_D^{23}$ 104.1 (*c* 5.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 6.15 (ddd, *J*1=*J*2=7.5 Hz, *J*3=1.5 Hz, 1H); 5.98 (br s, 1H); 4.05–3.96 (m, 2H); 3.46–3.35 (m, 2H); 3.11–3.04 (m, 2H); 2.37 (s, 3H); 2.12–2.04 (m, 2H); 2.06 (s, 3H); 1.94 (ddd, *J*1=12.5 Hz, *J*2=4.5 Hz, *J*3=2.5 Hz, 1H); 1.88–1.80 (m, 1H); 1.70–1.61 (m, 1H); 1.59–1.49 (m, 1H) 1.38–1.30 (m, 1H); 0.91 (d, *J*1=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 172.4, 140.9, 94.1, 82.7, 79.6, 62.1, 41.1, 38.6, 33.0, 32.0, 27.64, 27.60, 23.2, 13.0. LRMS (ESI) calcd for C₁₄H₂₄NO₂INa [M+Na] 404.07, found 404.09.



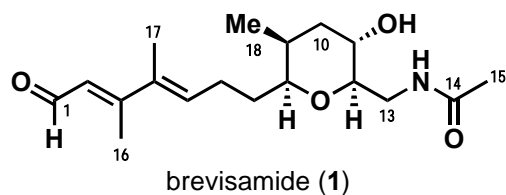
***N*-(((2R,3S,5S,6S)-3-Hydroxy-6-((3E,5E)-7-hydroxy-4,5-dimethylhepta-3,5-dien-1-yl)-5-methyltetrahydro-2H-pyran-2-yl)methyl)acetamide (2.71).** Vinyl stannane **2.59**⁷² (56.0 mg, 0.155 mmol, 5.0 equiv.) in a 1:1 v/v solution of THF and dimethylsulfoxide (3.40 mL) was added to a solution of substrate **14** (14.1 mg, 37.0 μ mol) in a 1:1 v/v solution of THF and dimethylsulfoxide (1:1, 0.60 mL) at rt. Copper(I) bromide-dimethylsulfide complex (81.0 mg, 0.394 mmol, 12.7 equiv.); triphenylarsenic (7.7 mg, 25.1 μ mol, 0.8 equiv.); and Pd₂(dba)₃ (2.8 mg, 3.1 μ mol, 0.8 equiv.) were added sequentially to the reaction vessel at rt and stirred for 1 h. diH₂O (4 mL) was added to the reaction vessel at rt and stirred for 20 min. The reaction vessel was filtered through Celite and washed with ethyl acetate (30 mL total with rinses). The collected organic phases were washed with diH₂O (20 mL); brine (20 mL); dried over sodium sulfate, and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 60% ethyl acetate – hexanes to 80% ethyl acetate – hexanes to 100% ethyl acetate to 5% methanol - ethyl acetate) and fractions containing product **2.71** were collected and concentrated *in vacuo*. The residue was purified again to remove traces of the vinyl stannane **2** by column chromatography (silica, 60% ethyl acetate – hexanes to 80% ethyl acetate – hexanes to 100% ethyl acetate to 5% methanol - ethyl acetate) delivering product **14** (9.4 mg, 28.9 μ mol, 78%). $[\alpha]_D^{23}$ 92.4 (c 2.0, CHCl₃). ¹H NMR (500 MHz, CD₃OD); δ (ppm): 8.01 (br s, 1H); 5.65 (dd, *J*₁=*J*₂=6.5 Hz, 1H); 5.60 (dd, *J*₁=*J*₂=6.5 Hz, 1H); 4.22 (d, *J*=6.5 Hz, 2H); 3.58–3.53 (m, 1H); 3.45–3.38 (m, 2H); 3.36–3.32 (m, 1H);

3.08 (ddd, $J_1=9.50$ Hz, $J_2=6.50$ Hz, $J_3=2.5$ Hz, 1H); 2.34–2.16 (m, 2H); 1.97 (s, 3H); 1.92 (ddd, $J_1=12.5$ Hz, $J_2=4.5$ Hz, $J_3=2.5$ Hz, 1H); 1.87–1.82 (m, 1H); 1.81 (s, 3H); 1.80 (s, 3H); 1.66–1.57 (m, 2H); 1.43–1.33 (m, 1H); 0.97 (d, $J_1=7$ Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD); $\delta(\text{ppm})$: 173.9, 139.5, 137.7, 128.0, 125.8, 83.2, 80.5, 65.1, 60.2, 42.7, 41.0, 34.3, 33.9, 26.2, 22.6, 14.4, 14.3, 13.2. LRMS (ESI) calcd for $\text{C}_{18}\text{H}_{31}\text{NO}_4\text{Na}$ $[\text{M}+\text{Na}]$ 348.22, found 348.30.



(+)-Brevisamide (2.2). (Diacetoxyiodo)benzene (7.4 mg, 23.0 μmol , 1.5 equiv.) in dichloromethane (0.600 mL) was added dropwise to a solution of substrate **2.71** (4.8 mg, 14.7 μmol) and TEMPO (1.2 mg, 7.7 μmol , 0.5 equiv.) in CH_2Cl_2 (0.600 mL) at rt and was stirred for 2 h. The reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography (silica, 2.5% methanol - chloroform) delivering (+)-brevisamide **2.2** (4.3 mg, 13.3 μmol , 90%). $[\alpha]_{\text{D}}^{23}$ 15.5 (c 1.0, MeOH) ^1H NMR (500 MHz, CD_3OD); $\delta(\text{ppm})$: 10.10 (d, $J_1=8.5$ Hz, 1H); 6.24 (dd, $J_1=J_2=7.5$ Hz, 1H); 6.05 (d, $J_1=8.5$ Hz, 1H); 3.55 (dd, $J_1=14.5$ Hz, $J_2=3.0$ Hz, 1H); 3.46–3.38 (m, 2H); 3.37–3.33 (m, 1H); 3.09 (ddd, $J_1=9.5$ Hz, $J_2=7.0$ Hz, $J_3=3.0$ Hz, 1H); 2.40 – 2.32 (m, 1H); 2.34 (s, 3H); 1.97 (s, 3H); 1.92 (ddd, $J_1=12.5$ Hz, $J_2=5.0$ Hz, $J_3=2.5$ Hz, 1H); 1.88 (s, 3H); 1.87–1.82 (m, 1H); 1.71–1.58 (m, 2H); 1.50–1.42 (m, 1H); 0.98 (d, $J_1=7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD); $\delta(\text{ppm})$: 194.5, 173.9, 161.1, 137.4, 137.0, 126.4, 83.2, 80.5, 65.1, 42.7, 41.0, 34.4, 33.3, 27.0, 22.6, 14.7, 14.1, 13.2. LRMS (ESI) calcd for $\text{C}_{18}\text{H}_{29}\text{NO}_4\text{Na}$ $[\text{M}+\text{Na}]$ 346.20, found 346.23.

Table 1. Synthetic Brevisamide Spectral Data Compared to Natural Brevisamide Data



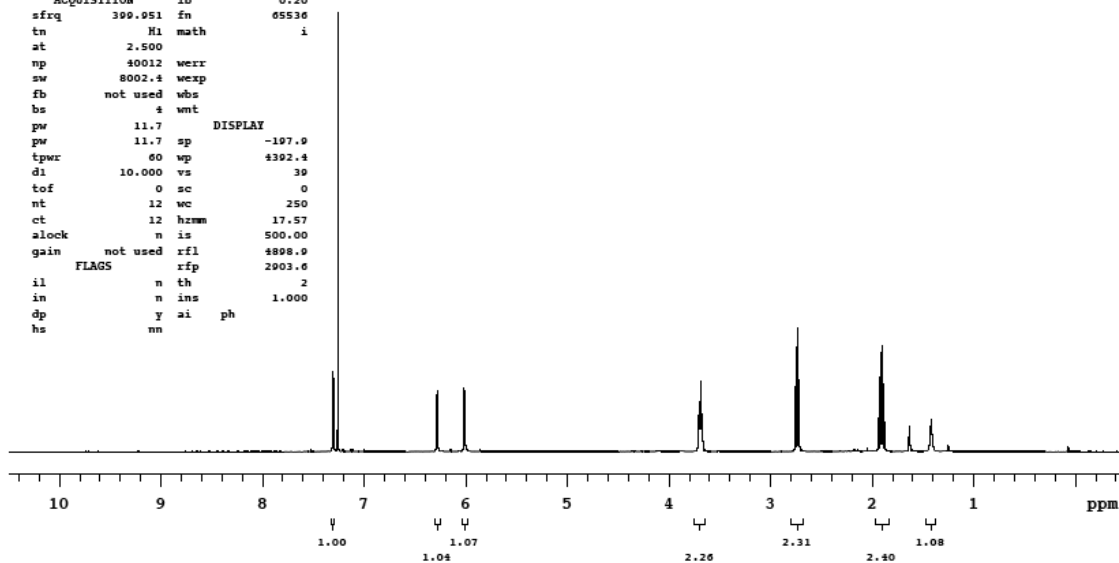
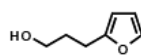
Position	¹ H NMR (mult, <i>J</i> in Hz)		¹³ C NMR	
	Synthetic	Natural	Synthetic	Natural
1	10.10 (d, 8.5)	10.10 (d, 7.9)	194.5	194.4
2	6.05 (d, 8.5)	6.04 (d, 7.9)	126.4	126.3
3			161.1	160.9
4			137.4	137.2
5	6.24 (dd, 7.5)	6.23 (t, 7.1)	137.0	136.8
6	2.36 m	2.34 m	27.0	26.9
7a	1.65 m	1.65 m	33.3	33.2
7b	1.46 m	1.44 m		
8ax	3.42 m	3.39 m	80.5	80.3
9eq	1.85 m	1.85 m	34.4	34.3
10eq	1.92 (ddd, 2.5, 5.0, 12.5)	1.90 m	41.0	40.9
10ax	1.65 m	1.65 m		
11ax	3.42 m	3.42 m	65.1	65.0
12a	3.09 (ddd, 3.0, 7.0, 9.5)	3.08 (ddd, 2.6, 7.0, 9.3)	83.2	83.1
13a	3.55 (dd, 3.0, 14.5)	3.53 (dd, 2.6, 14.0)	42.7	42.5
13b	3.35 m	3.32 (dd, 7.1, 14.0)		
14			173.9	173.7
15	1.97 s	1.95 s	22.6	22.5
16	2.34 s	2.33 s	14.7	14.6
17	1.88 s	1.86 s	14.1	14.0
18	0.98 (d, 7.0)	0.95 (d, 6.9 Hz)	13.2	13.1

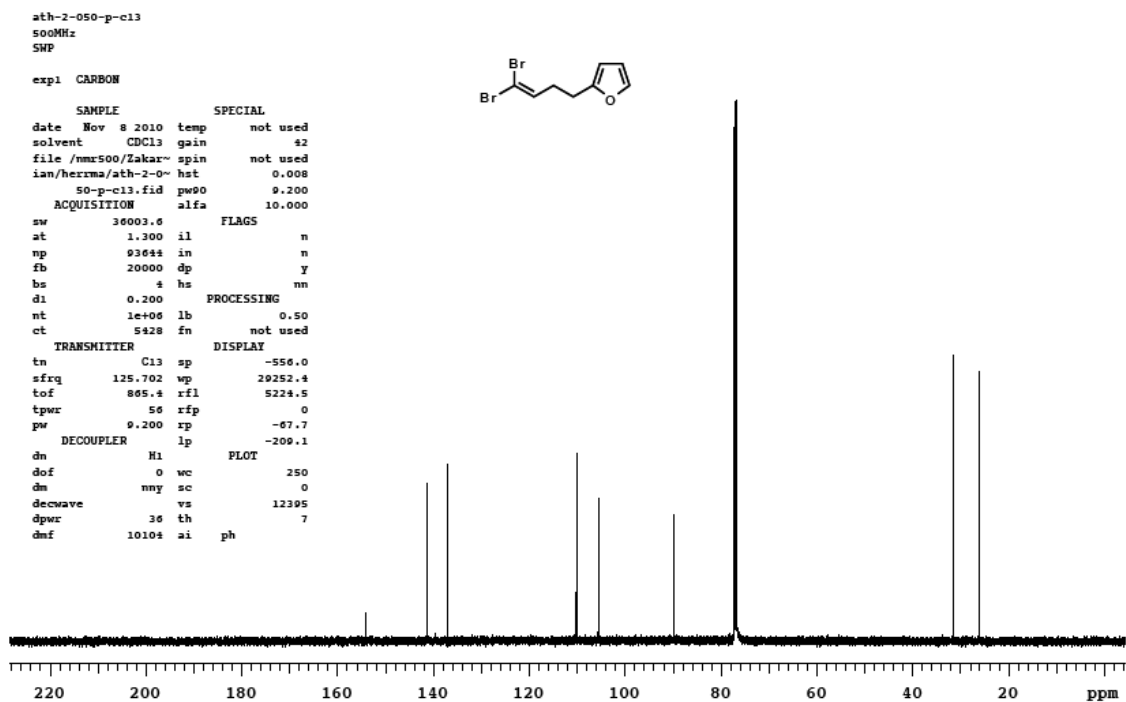
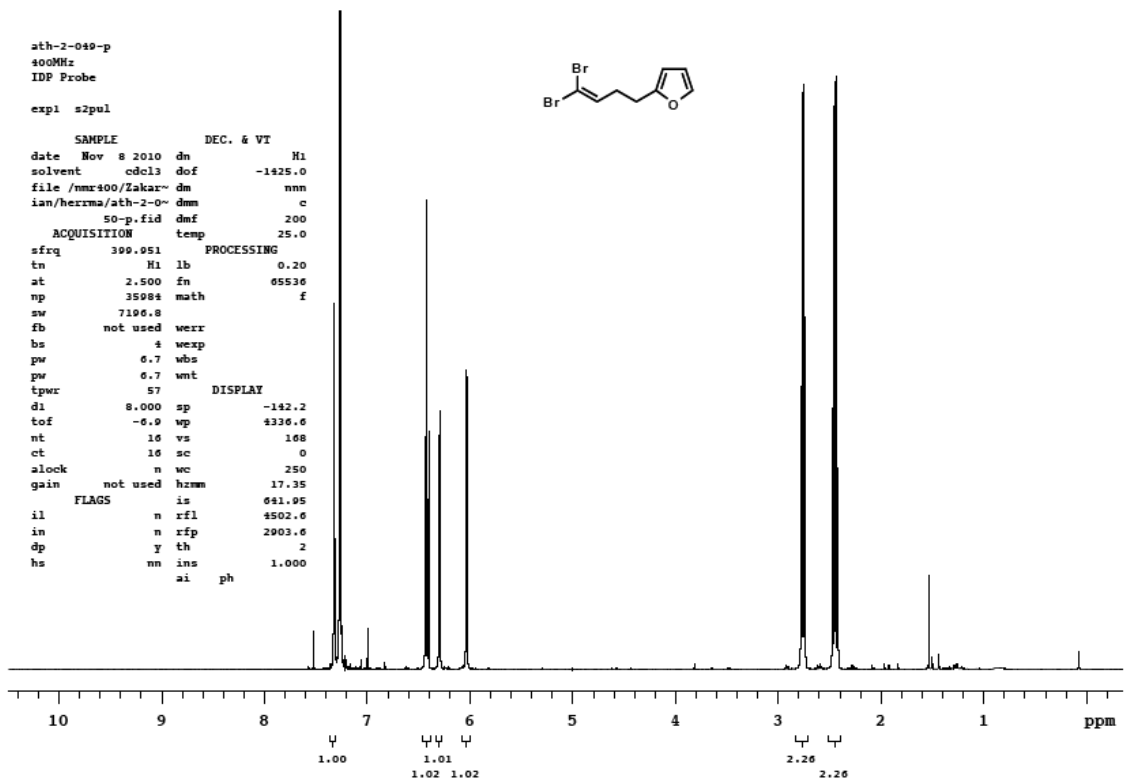
¹H NMR: Synthetic at 500 MHz; Natural at 500 MHz in CD₃OD
¹³C NMR: Synthetic at 125 MHz; Natural at 125 MHz in CD₃OD

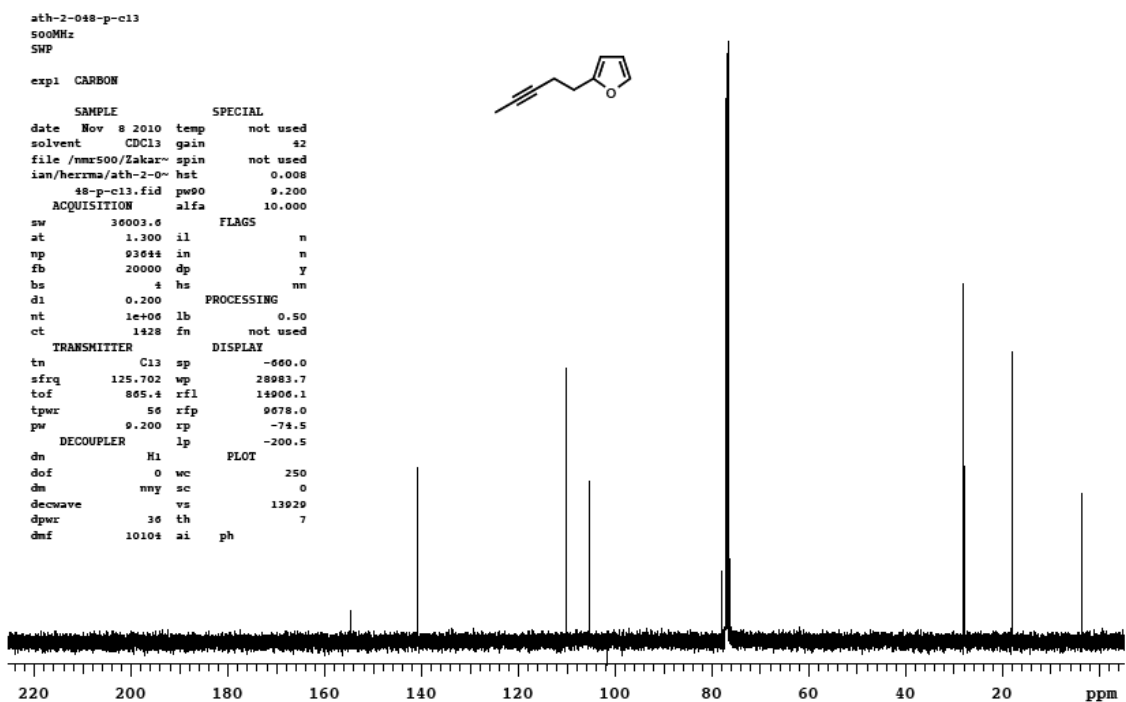
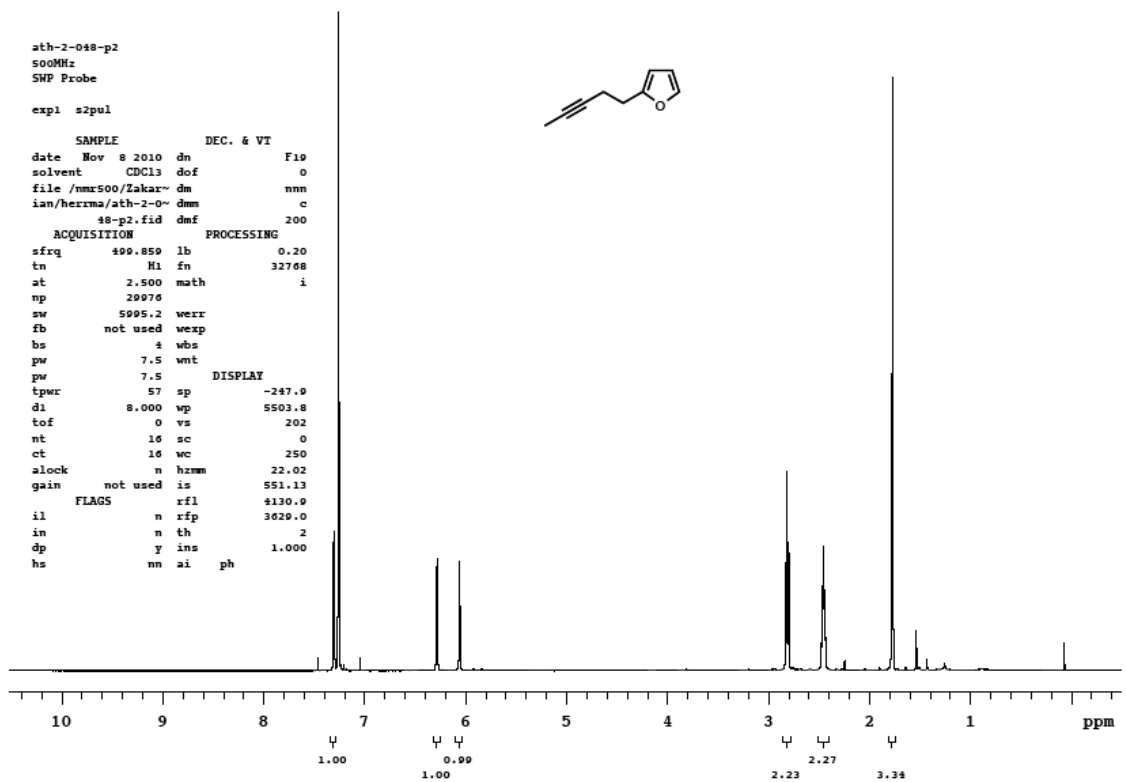
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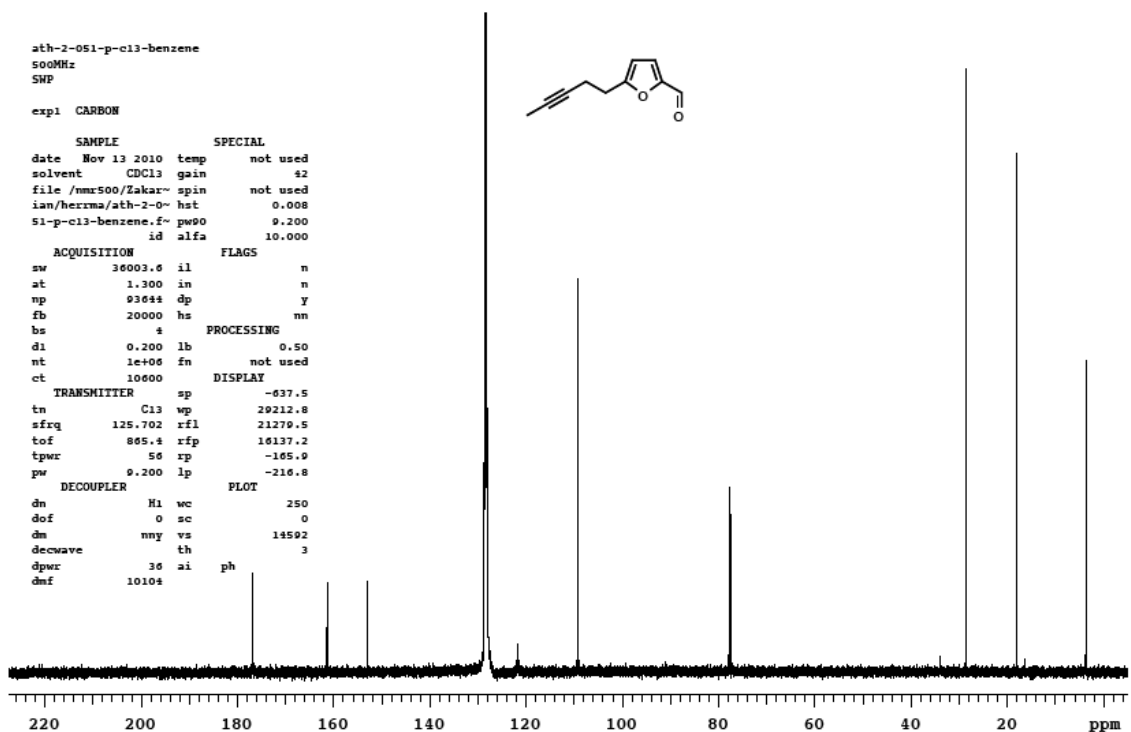
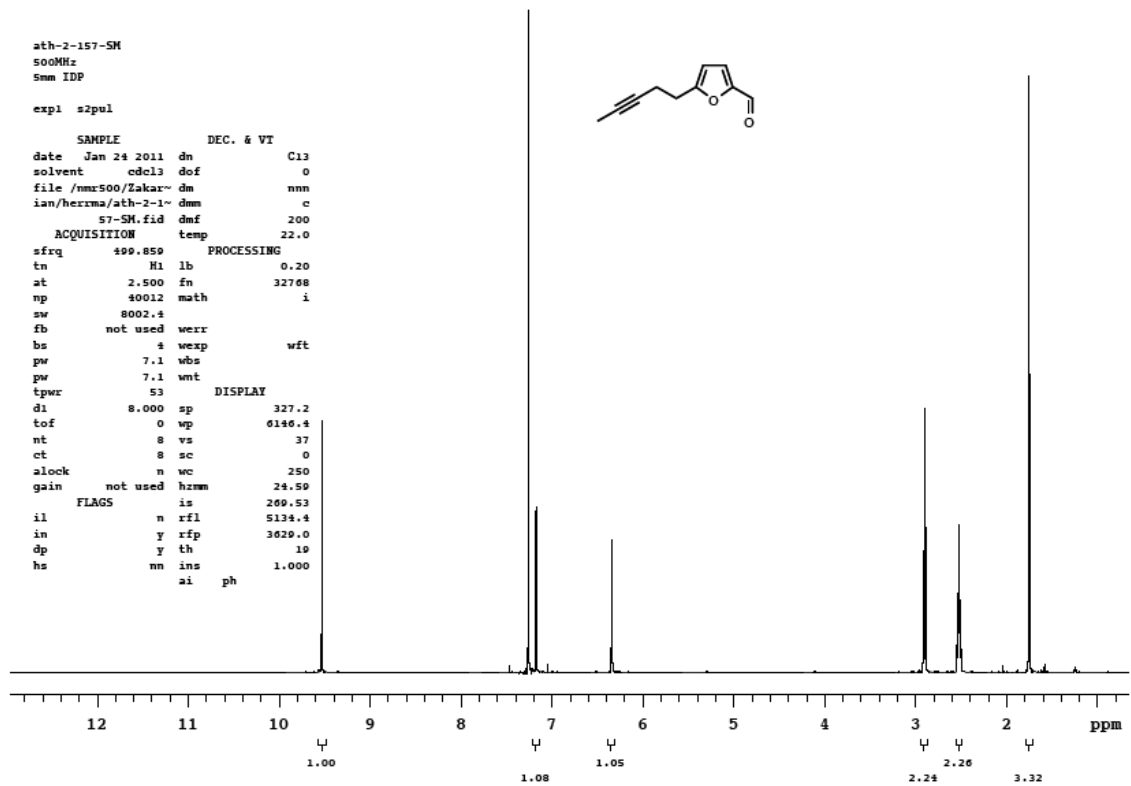
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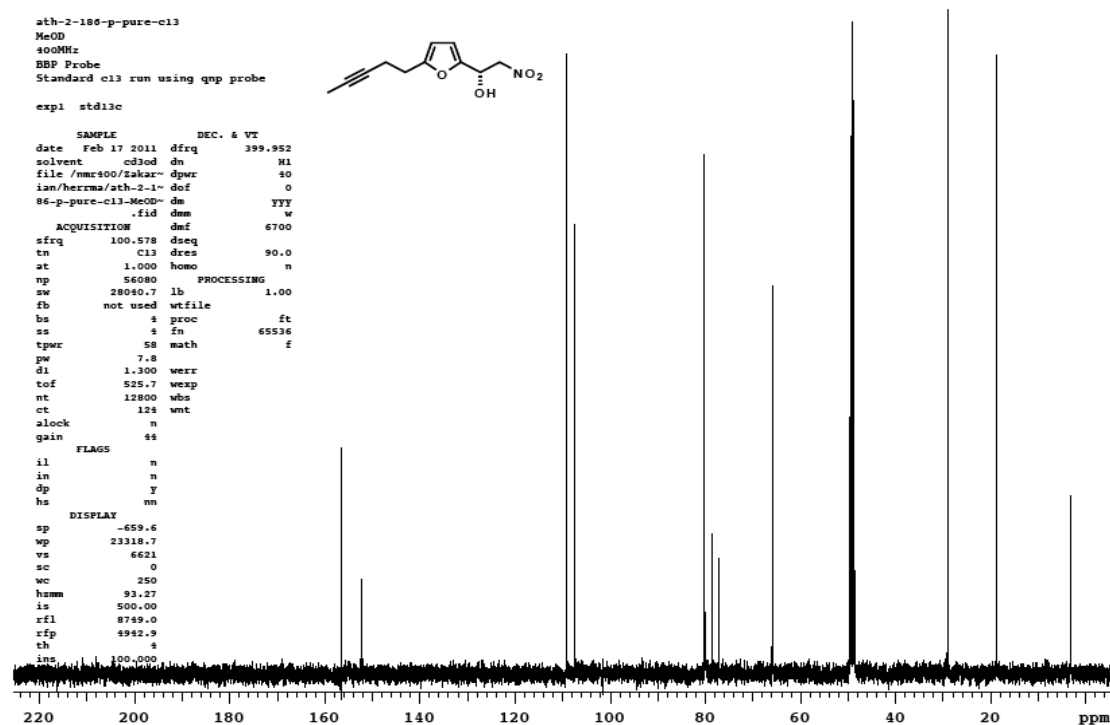
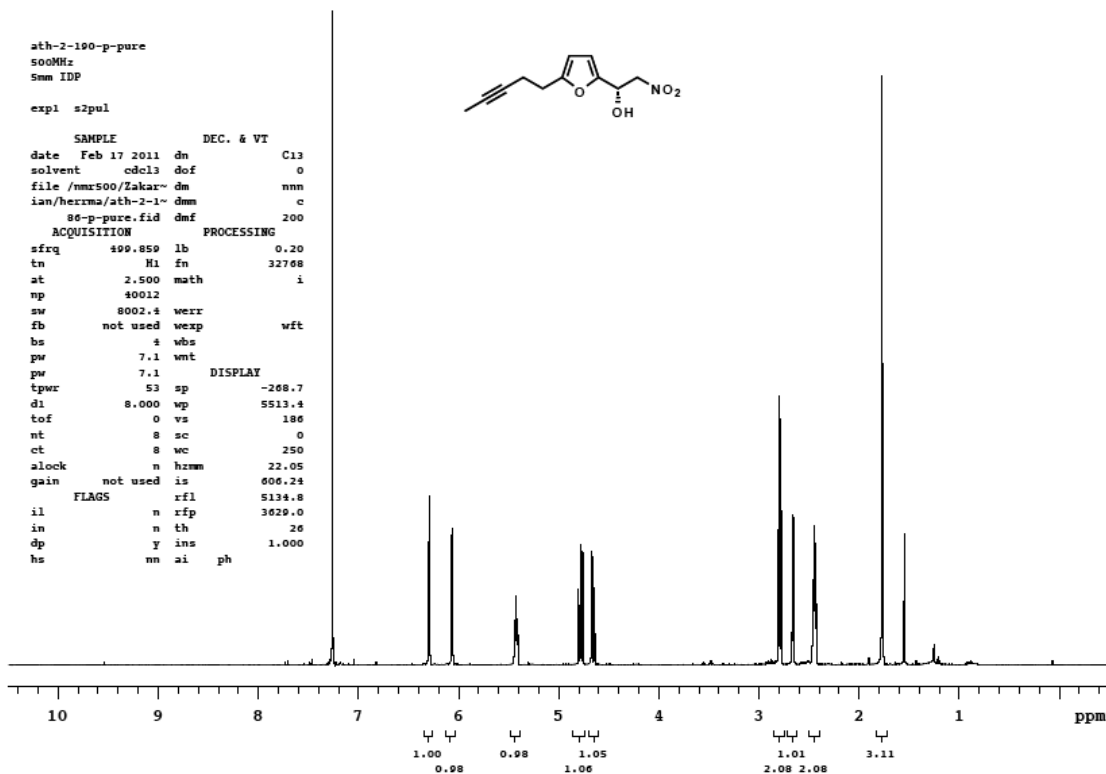
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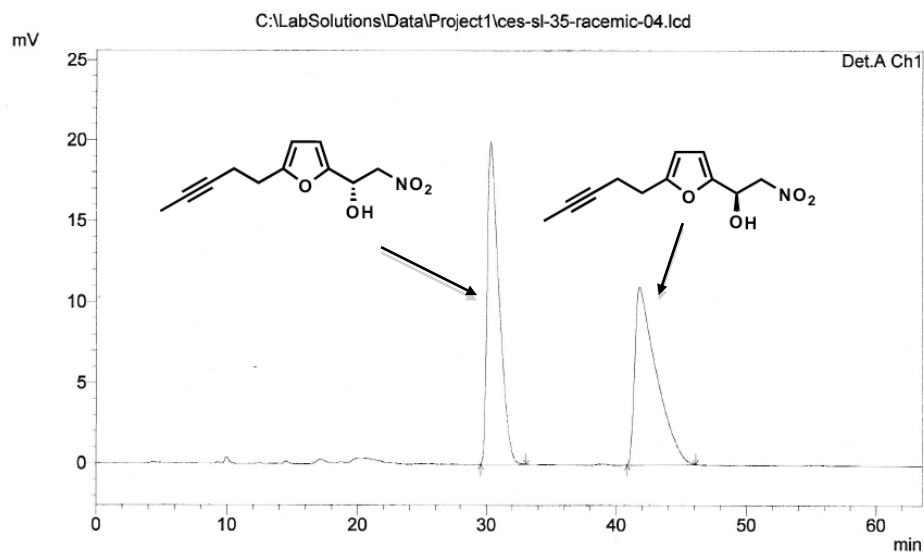






==== Shimadzu LCsolution LC Data Image ====

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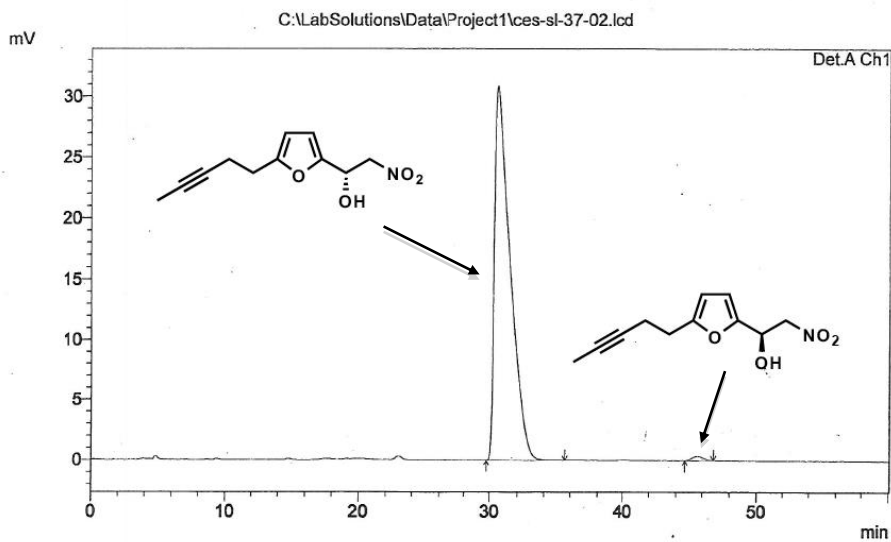
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==== Shimadzu LCsolution LC Data Image ====

<Chromatogram>



Sample Information

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PeakTable

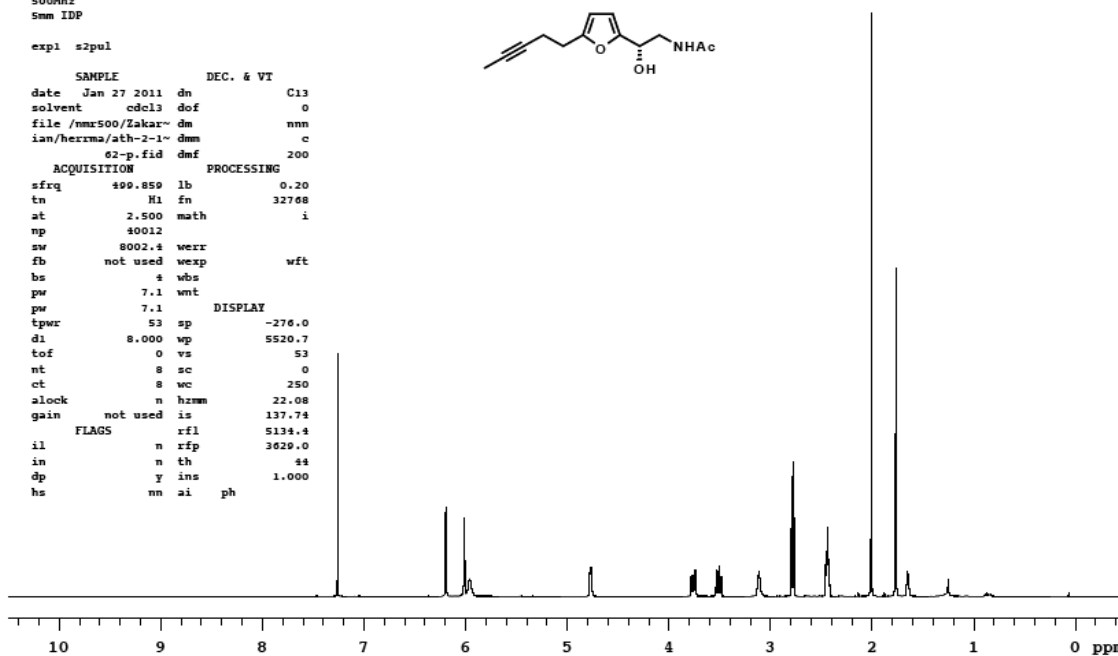
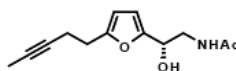
Detector A Ch1 215nm

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expt s2pul

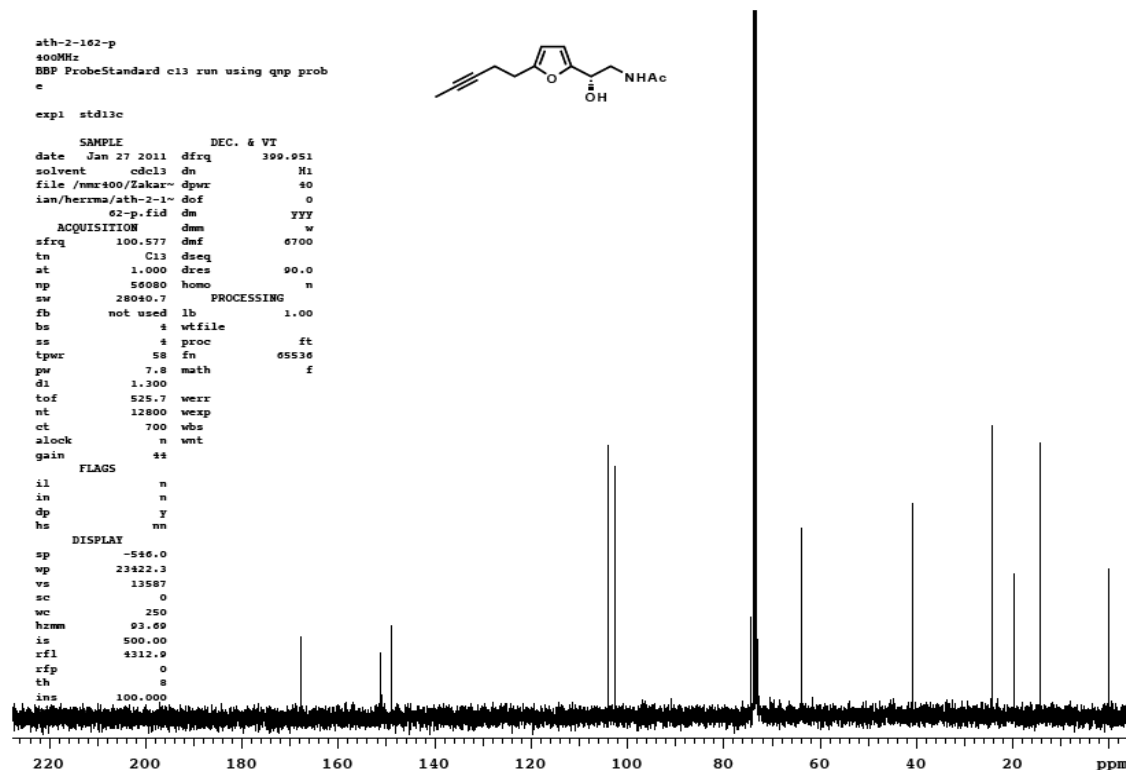
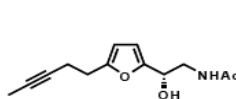
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BBP ProbeStandard c13 run using qnp prob
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expt std13c

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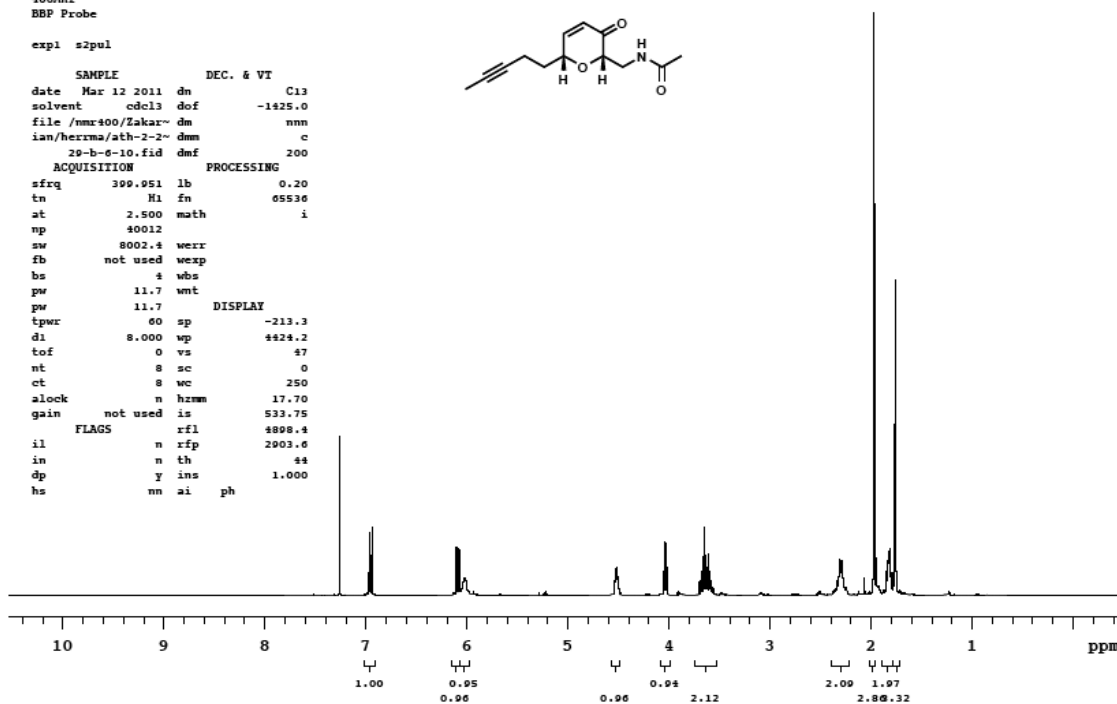
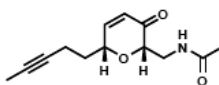
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expi s2pul

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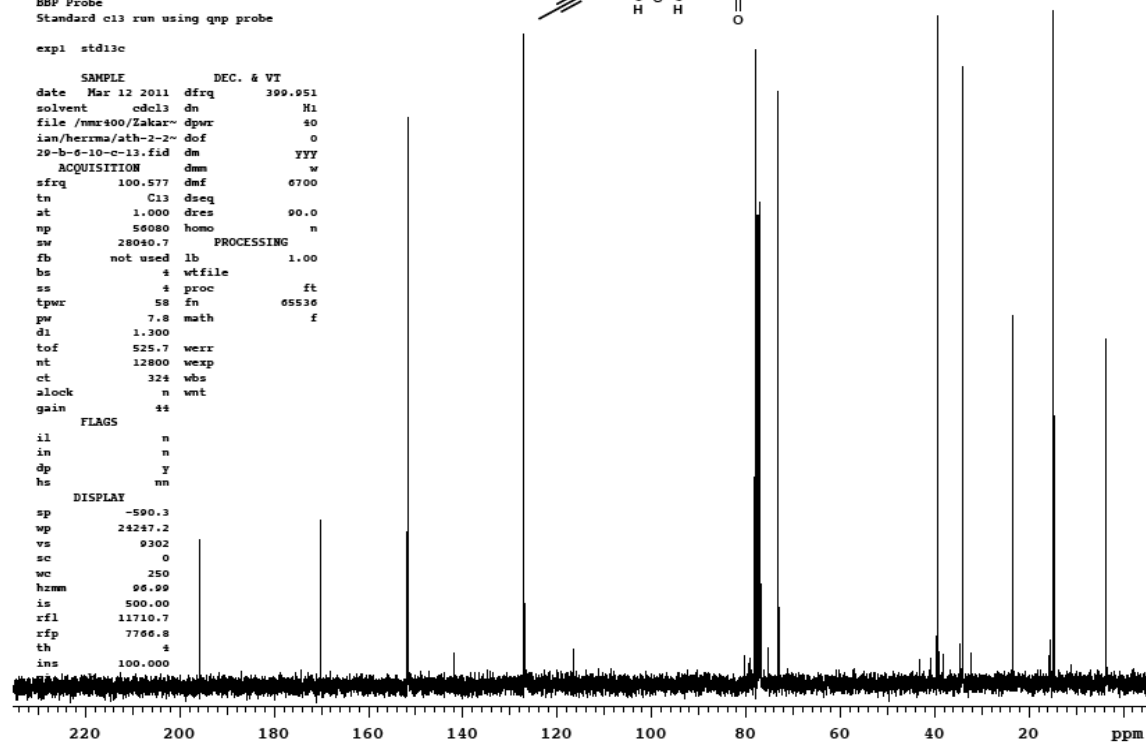
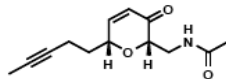
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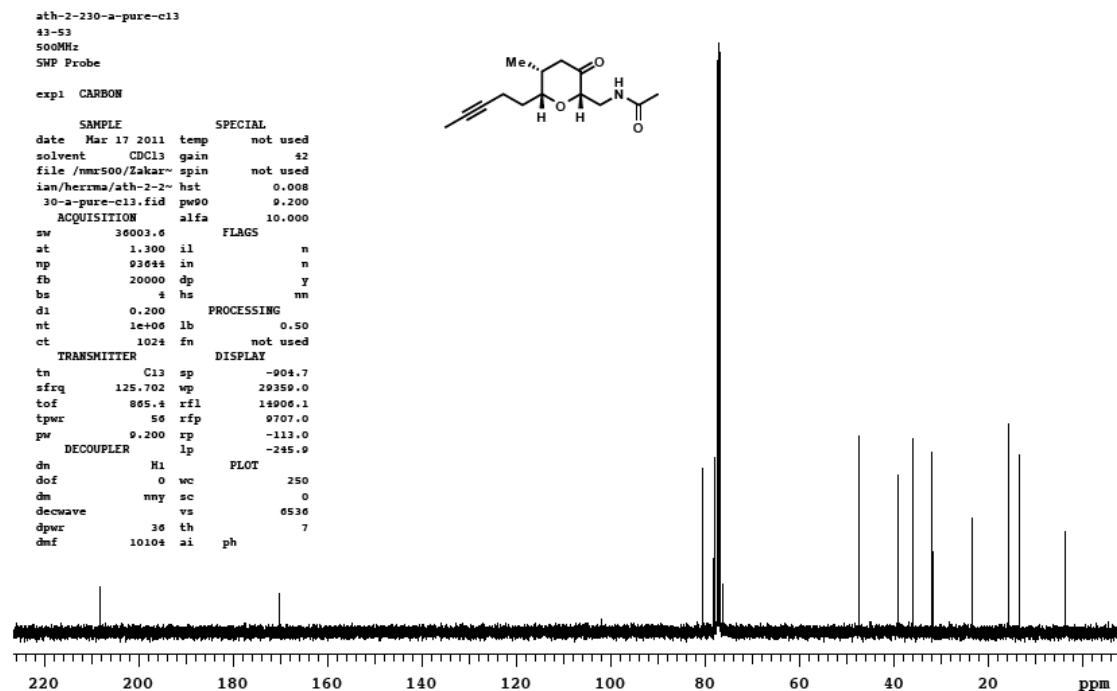
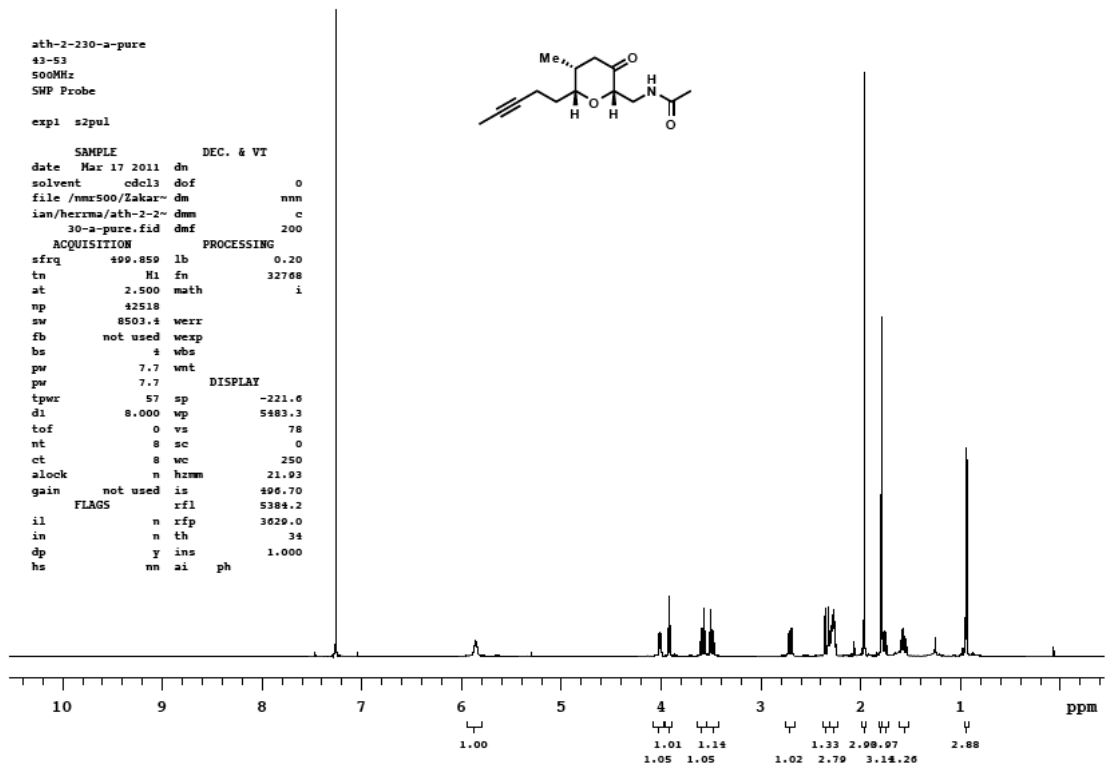
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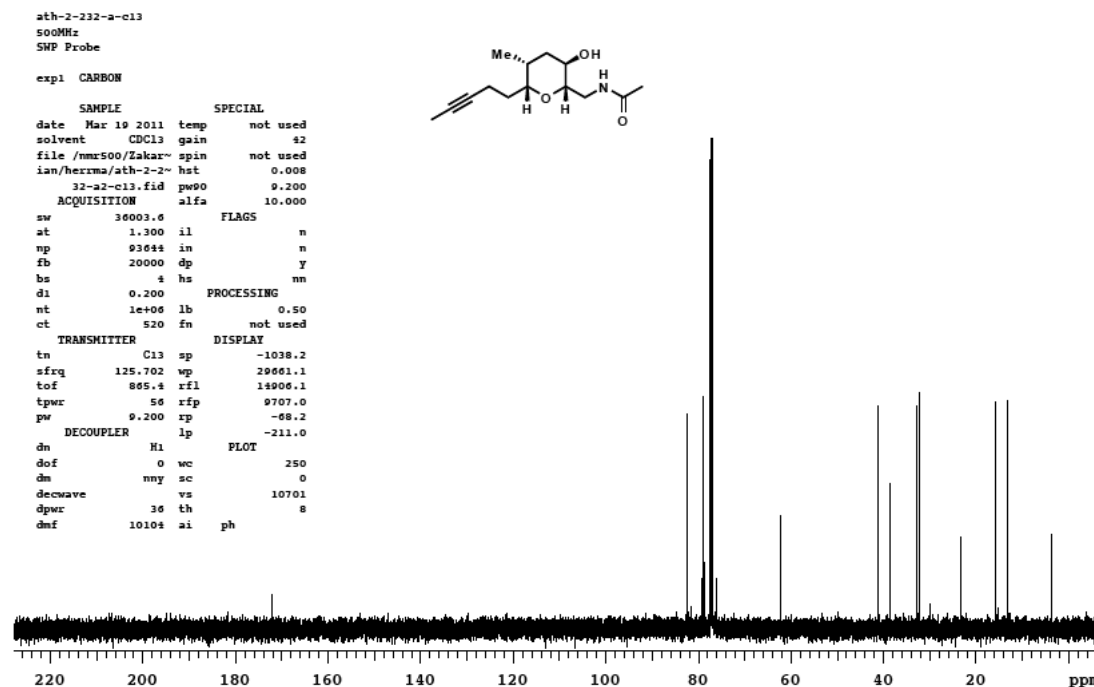
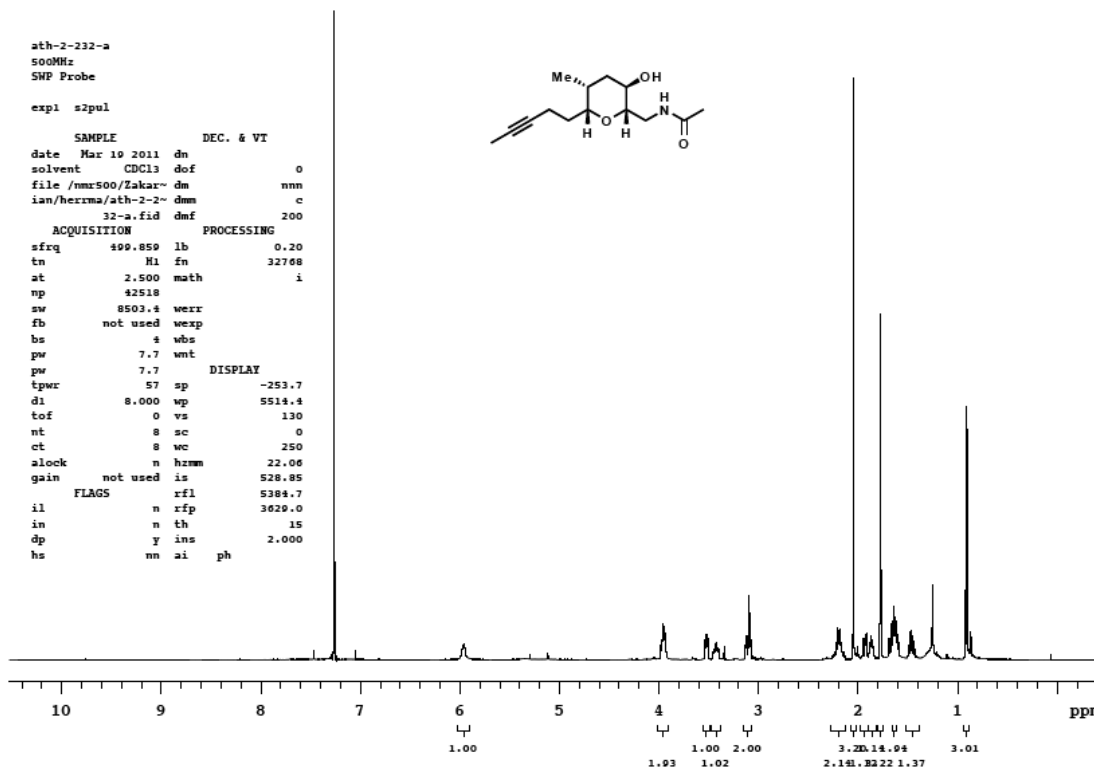
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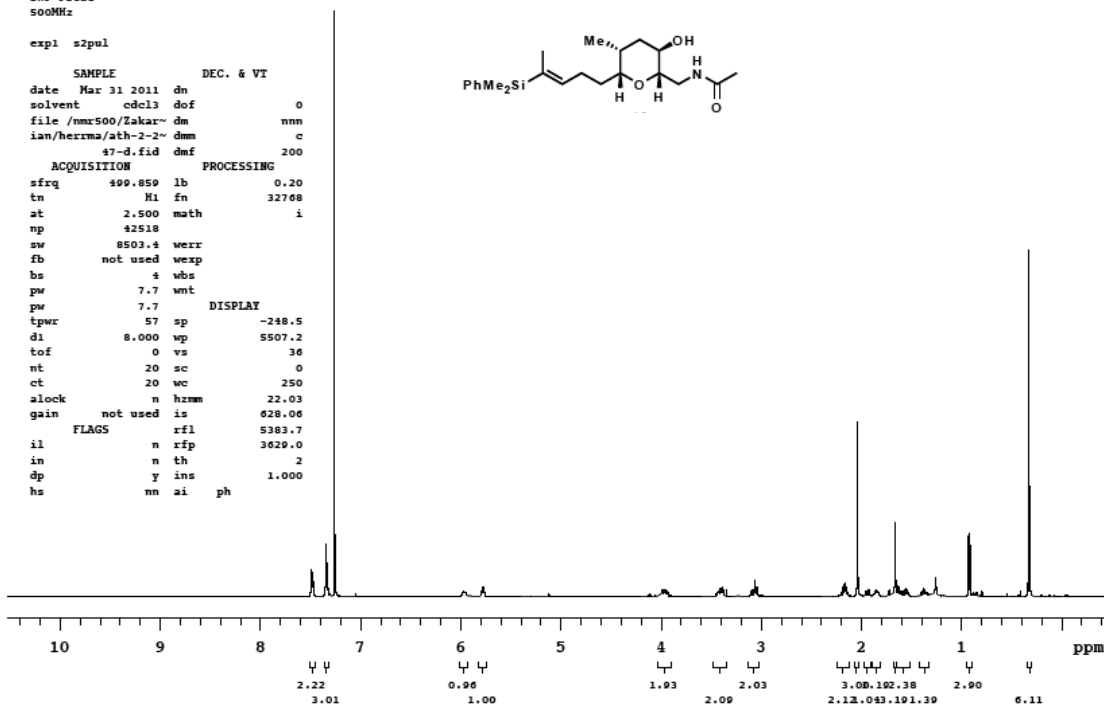
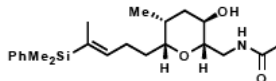


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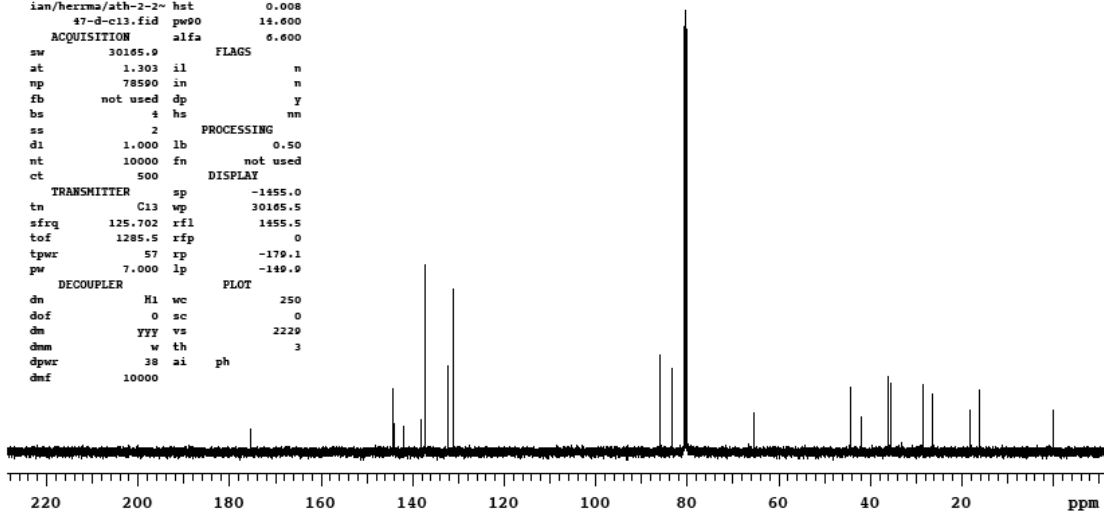
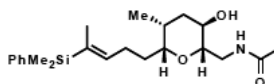
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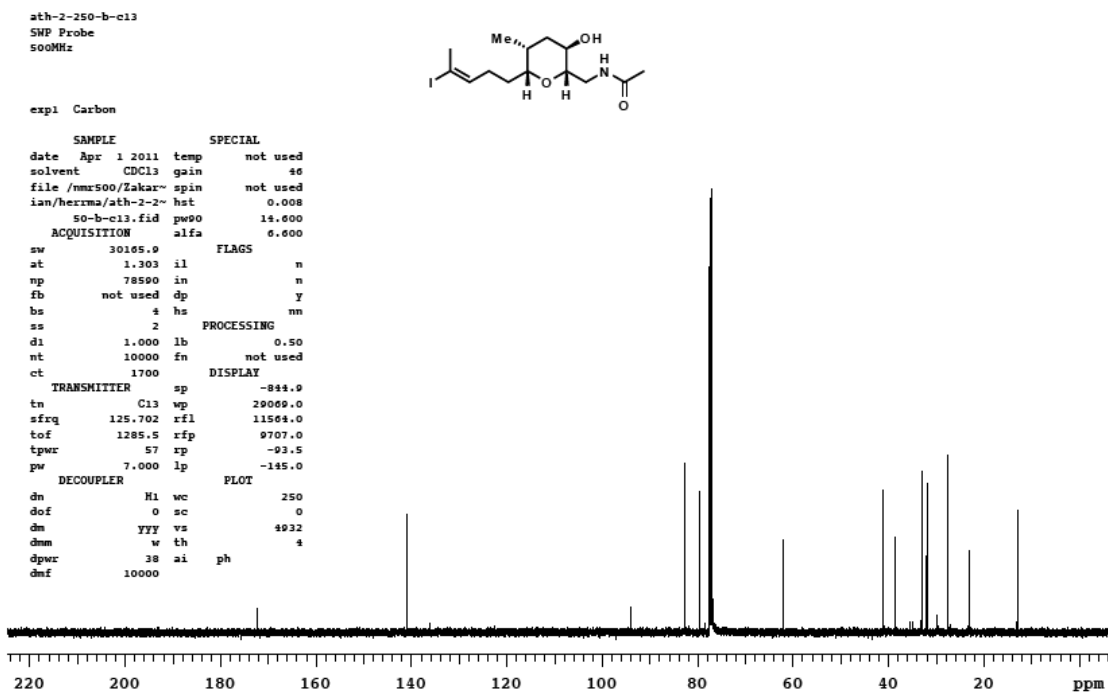
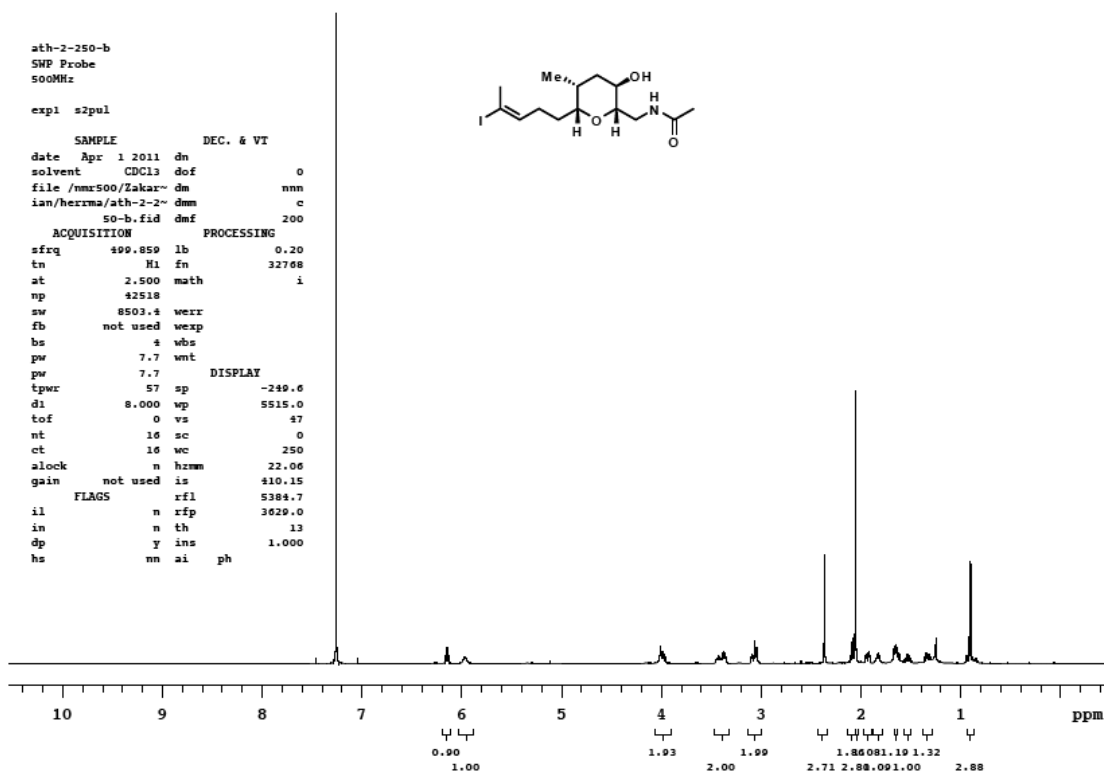


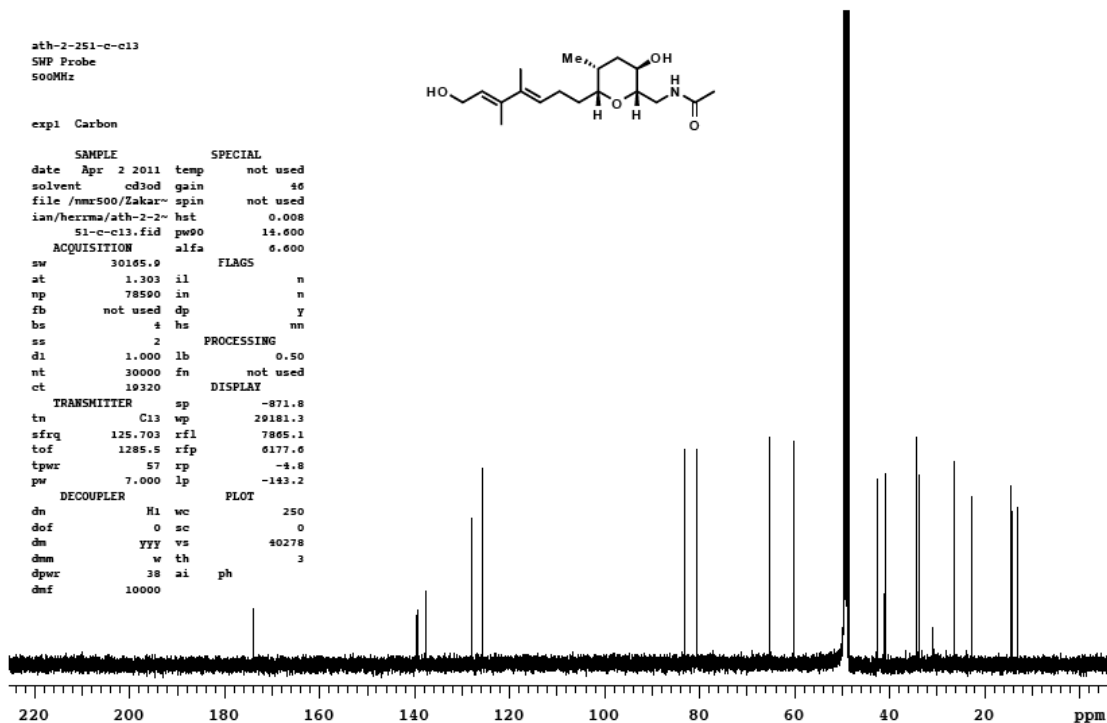
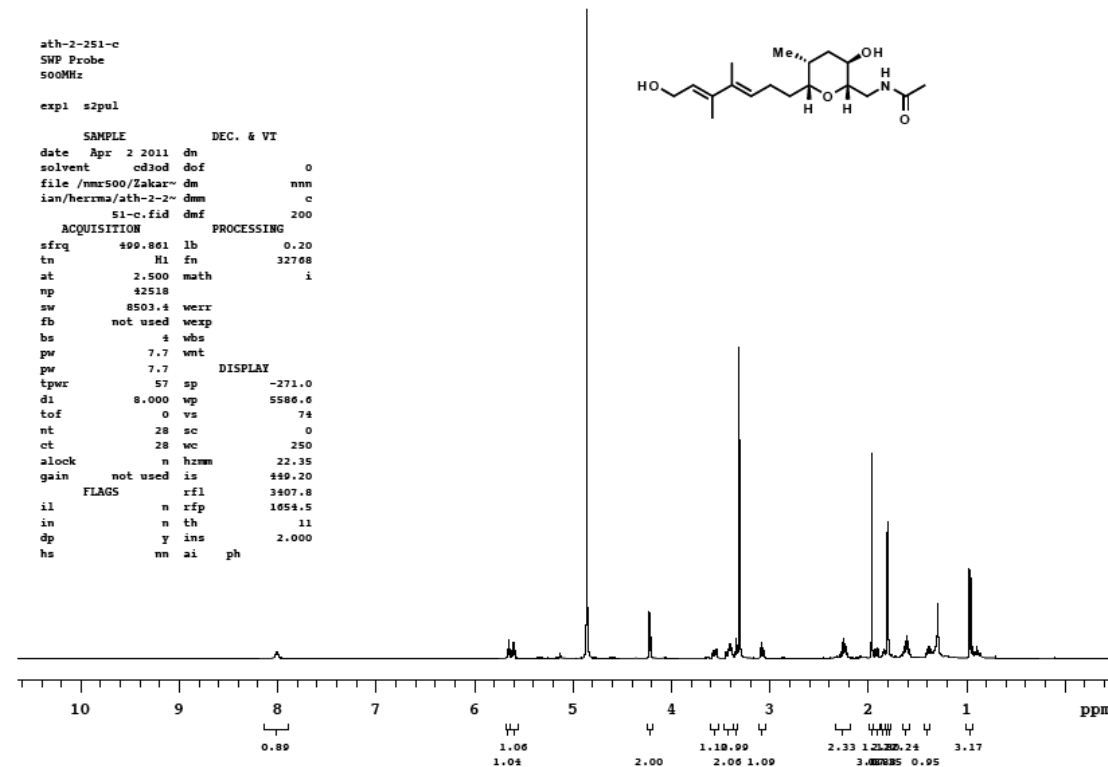
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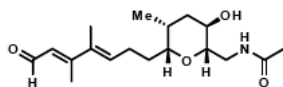




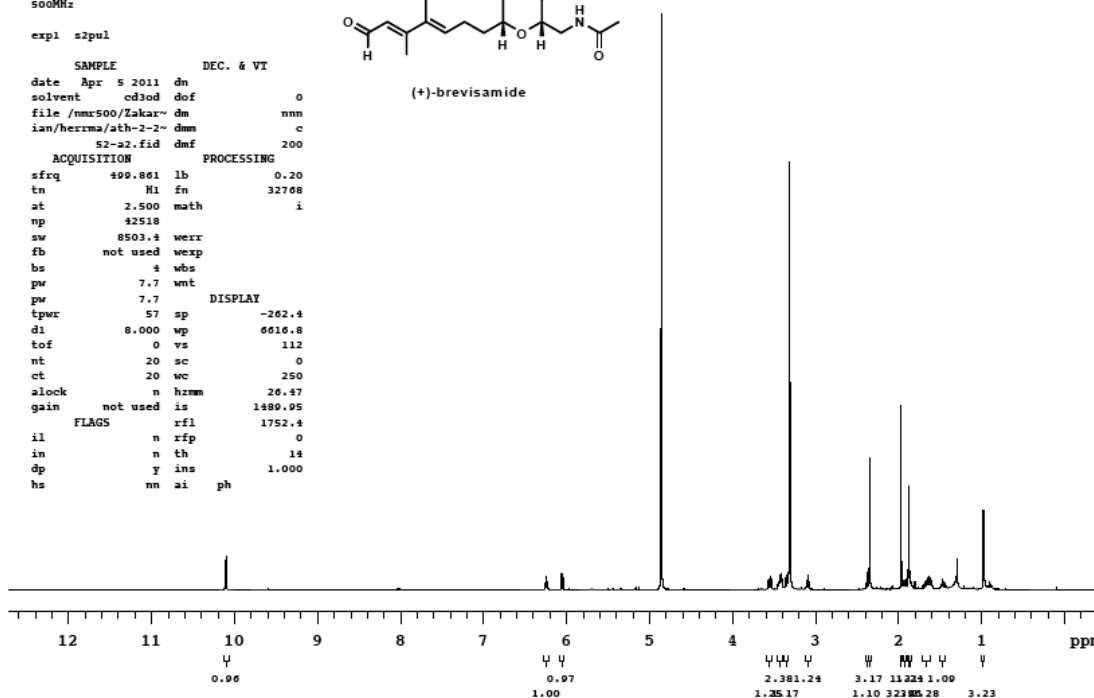
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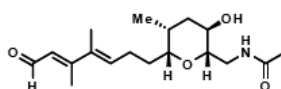
(+)-brevisamide



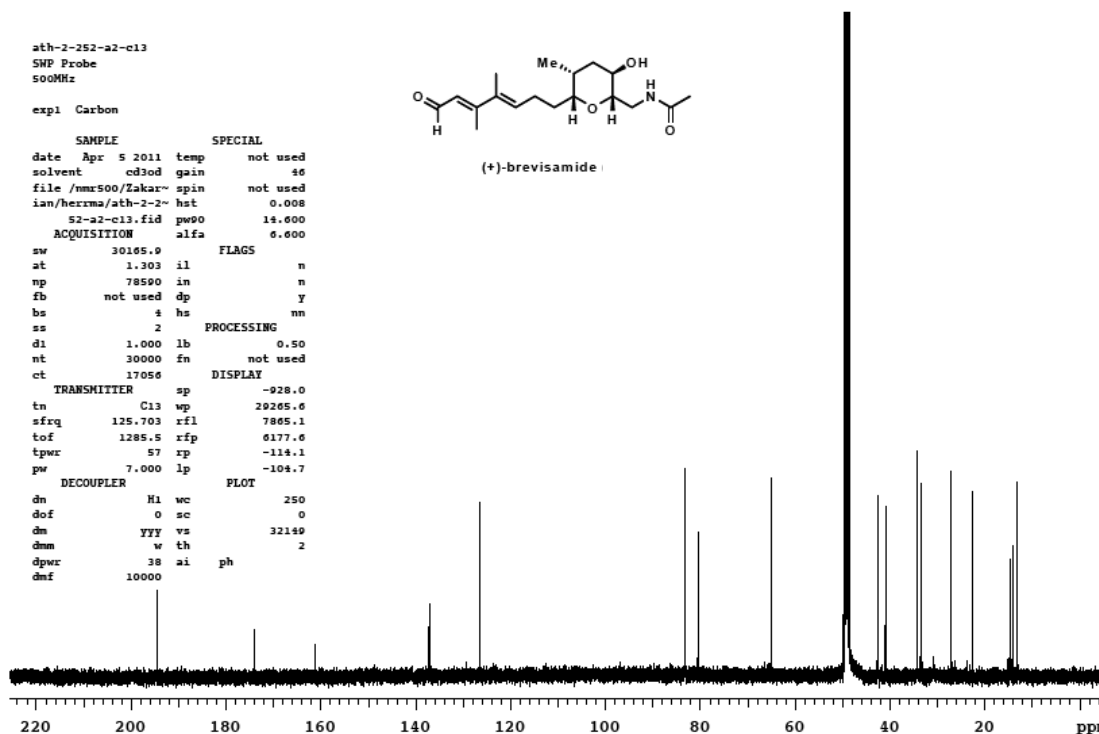
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(+)-brevisamide



Chapter 3

Haloalkylations of *N*-Acyl Oxazolidinones via Group IVa Metal Enolates

3-1 Halogenated Natural Products

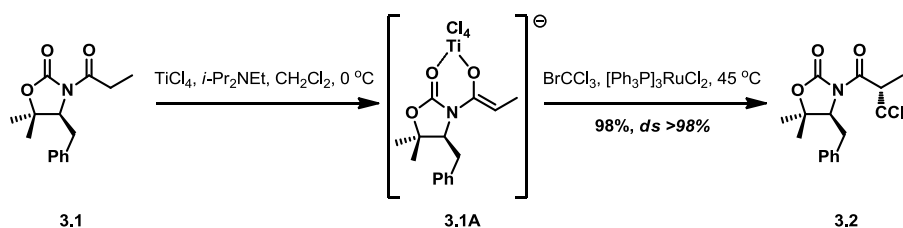
Recently there has been a mounting realization of the advantage in both the unique physical and chemical properties of a wide variety of halogenated organic compounds. An increasingly broad application of these compounds can in turn be used in many areas of research: natural product synthesis, medicinal, materials sciences, and agrochemicals are a few among the many. Due to this reason, new synthetic methods have been and must be developed in order to introduce halogens into a variety of organic compounds. Our group focused on the development of synthetic methods for stereoselective haloalkylations in order to provide an overall practical, efficient, and operationally simple technique.

3-2 Trichloroalkylations via TiCl_4 Enolates

Titanium enolates have found widespread use in organic synthesis as a result of their unique reactivity and ease of preparation from inexpensive and nontoxic titanium reagents under mild conditions that are compatible with a range of functional groups.⁷³ The most prevalent application of titanium enolates is in stereoselective aldol reactions.⁷⁴ Several examples of the alkylation of titanium enolates with strongly electrophilic reagents have also been reported.⁷⁵ Valence tautomerism in titanium enolates provided the initial conceptual foundation for the development of direct radical chloroalkylation. Using studies completed by Moreira and co-workers allowed for the postulation that the unconventional biradical character of titanium enolates could allow them to act as efficient radical acceptors.⁷⁶

Titanium enolates can be formed from inexpensive and nontoxic titanium reagents, under mild conditions that are compatible with a range of functional groups. This strategy of soft-enolate formation was coupled with the Kharasch-type reaction involving Ru(II)-catalyzed redox of trichloromethyl bromide. Upon initial studies this proved true, when *N*-acyl oxazolidinone **3.1** was treated with TiCl₄ and Hünig's base (*i*-Pr₂NEt); Ti enolate **3.1A** was formed as evidenced by ¹H NMR (Scheme 3.2.1). Upon addition of BrCCl₃ in the presence of [(Ph₃P)₃RuCl₂], product **3.2** was obtained in nearly quantitative yield and excellent stereocontrol.⁷⁷

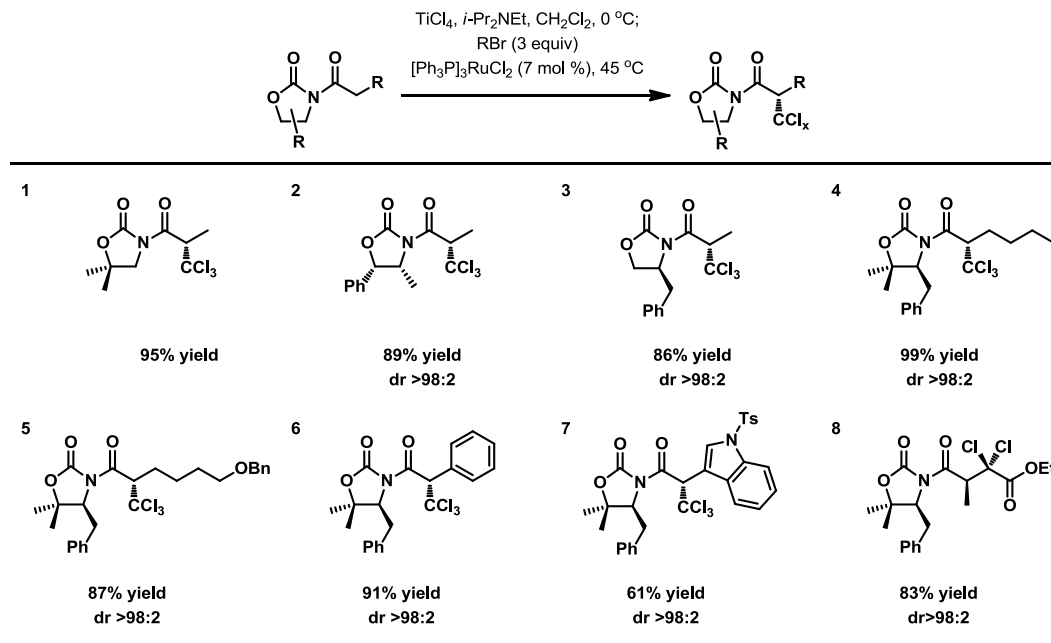
Scheme 3.2.1 Trichloromethylation of *N*-Acyl Oxazolidinones



The scope of direct chloroalkylation using the new titanium enolate derived synthetic method was carried out in which Table 3.2.1 demonstrates different Evans-type chiral auxiliaries and a wide variety of substituents on the *N*-acyl oxazolidinones. Aromatic, heterocyclic, along with alkyl substituents proved to be very compatible with the reaction conditions proceeding in high yields and high stereocontrol.

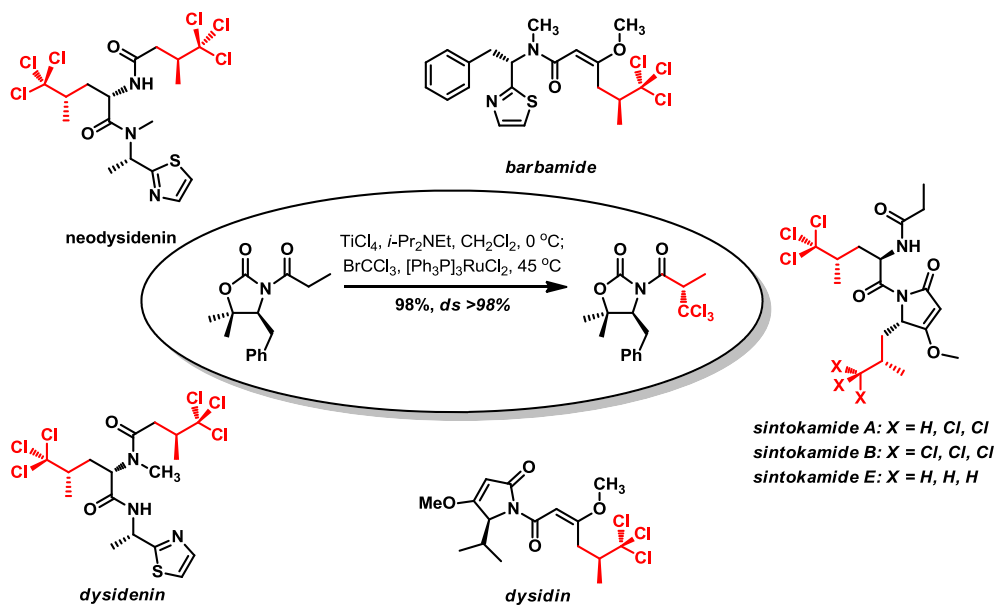
Application of trichloromethylation via titanium enolates was demonstrated by the Zakarian group in multiple total syntheses: neodysidenin, barbamide, dysidenin, dysidin, and sintokamides A, B, & E (Scheme 3.2.2).^{77,78} The high yield and excellent stereocontrol allowed for efficient use in each total synthesis.

Table 3.2.1 Radical Trichloromethylation: *N*-Acyl Oxazolidinone Scope



(a) All yields are of isolated products; dr determined by 500 MHz ^1H NMR of the crude mixture of products.

Scheme 3.2.2 Total Syntheses Applying Trichloromethylation Methodology

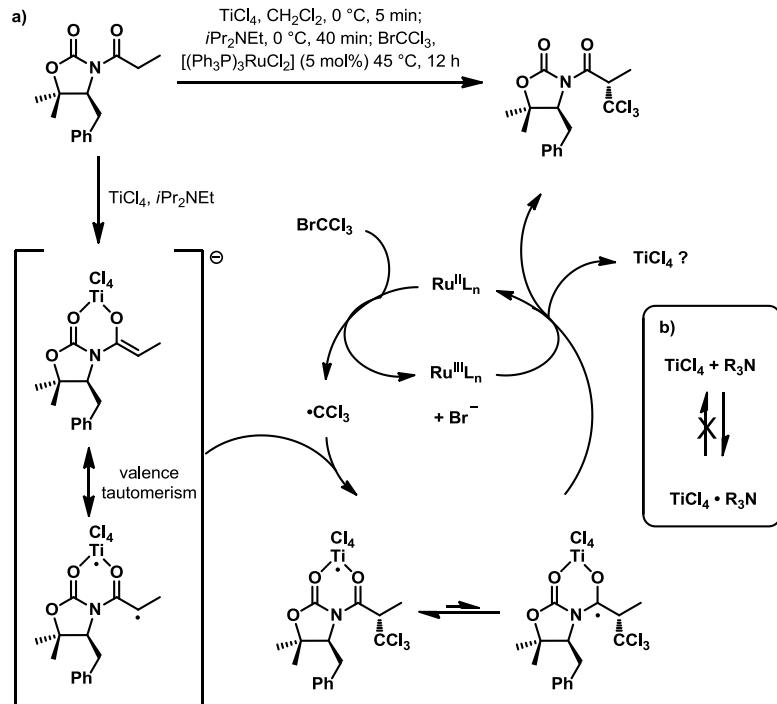


3-3 Dual Ti-Ru Catalysis in the Direct Radical Haloalkylation of *N*-Acyl Oxazolidinones

We described a different mode of alkylation of titanium enolates in which they serve as efficient radical acceptors for haloalkyl radicals generated by a ruthenium-catalyzed redox process (*vide supra*). It has been postulated that the enolate serves as an electroactive ligand for the titanium center,⁷⁹ whereby it facilitates the radical addition process and participates in the ruthenium catalytic cycle. The utility of this method in the synthesis of a range of chloroleucine-derived natural products has been illustrated.^{77,80} One intriguing aspect of the reaction that emerged during our investigations is the possibility of the catalytic generation and alkylation of the titanium enolate species. Herein, we describe the development of a haloalkylation process that is catalytic in both ruthenium and titanium and thus constitutes the first example of a catalytic enolate alkylation involving titanium enolates.

During an examination of the putative mechanism of the trichloromethylation process outlined in Scheme 3.3.1,^{77,79} we directed our attention toward the function of titanium tetrachloride. This mechanism suggests that TiCl_4 should be regenerated at the completion of the reaction, which creates potential for the development of a catalytic process. According to the seminal studies by Evans *et. al.*, initial complexation of the substrate and titanium tetrachloride is prerequisite to the addition of the amine base and the ensuing enolization.⁸¹ If the order of the reagent addition is reversed, enolization is precluded by the apparently irreversible formation of an unreactive TiCl_4 -amine adduct. Thus, the potential interception of the regenerated TiCl_4 by the amine base would be a major challenge in the catalytic recovery of the reagent.

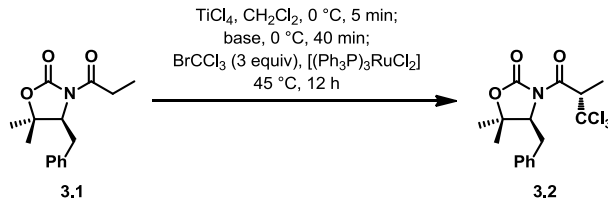
Scheme 3.3.1 Radical Trichloromethylation Mechanism



Radical Trichloromethylation Based on Valence Tautomerism in Titanium Enolates: a) an initial overview of the mechanism; b) potential sequestering of TiCl_4 by the amine.

Preliminary experimentation revealed that indeed the haloalkylation reaction could reach completion with substoichiometric titanium tetrachloride under the original reaction conditions with diisopropylethylamine (Hünig's base). On the other hand, the conversion decreased precipitously when less than 0.3 equivalents of TiCl_4 were used (Table 3.3.1, entries 1–4). We hypothesized that the decline in conversion at around 0.3–0.4 equivalents of TiCl_4 could be attributed to one of the following factors: 1) the possible formation of higher-order titanium enolates with a 2:1 or 3:1 ligand-to-metal ratio, in which case no catalytic turnover of TiCl_4 would occur, or 2) inefficient catalytic recovery of the titanium reagent and, possibly, a strong inhibitory effect by the amine.

Table 3.3.1 Amine Influence on the Course of the Catalytic Trichloromethylation Reaction



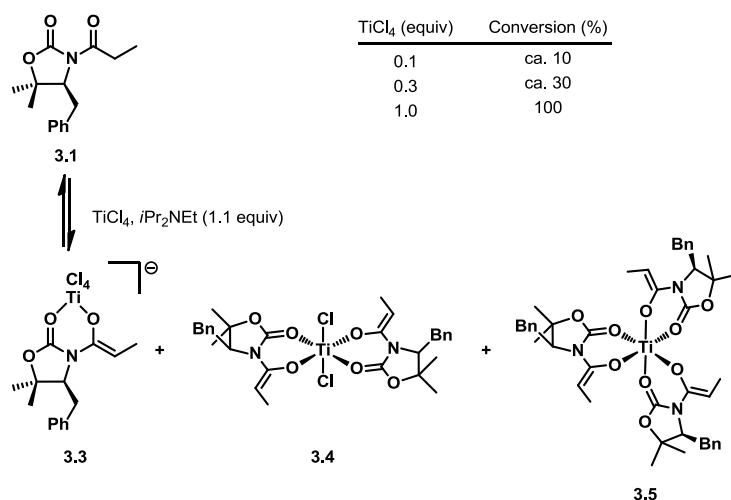
Entry	TiCl ₄ (mol %)	Amine (equiv)	Conversion (%)
1	40	<i>i</i> Pr ₂ Net (1.1)	> 95
2	30	<i>i</i> Pr ₂ Net (1.1)	75
3	20	<i>i</i> Pr ₂ Net (1.1)	50
4	10	<i>i</i> Pr ₂ Net (1.1)	14
5	30	<i>i</i> Pr ₂ Net (3.0)	47
6	30	<i>i</i> Pr ₂ Net (4.5)	28
7	30	Et ₃ N (1.1)	76
8	30	Et ₃ N (3.0)	100
9	10	Et ₃ N (3.0)	75
10	10	Et ₃ N (3.0)	74
11	10	Et ₃ N (4.5)	76
12	30	PMP (1.1)	100
13	10	PMP (1:1)	100

(a) Conversion was determined by ¹H NMR spectroscopy of the crude mixture of products. (b) The reaction time was 48 h. PMP = 1,2,2,6,6-pentamethylpiperidine.

Although it is well-known that titanium forms hexa- or octa-coordinated complexes,⁸² higher-order titanium enolates such as those depicted in Scheme 3.3.2 have not been documented. We monitored the enolization reaction with the Hünig's base (1.1 equiv) and varying amounts of titanium tetrachloride by NMR spectroscopy and found no conclusive support for the existence of higher-order titanium enolates; however, it was evident that the

degree of enolization diminished proportionally with decreasing substoichiometric amounts of TiCl_4 . Thus, whereas complete enolization was observed with 1.0 equivalent of TiCl_4 , the conversion was approximately 10% with 0.1 equivalents of TiCl_4 and about 30% with 0.3 equivalents of TiCl_4 . Notably, it could be clearly observed that more than one distinct enolate species was generated, and the relative ratios changed substantially as the amount of the titanium reagent was varied. Although the nature of the additional species is presently unclear,⁸³ we concluded that full conversion in the trichloromethylation reaction with a substoichiometric amount of TiCl_4 could not be rationalized through the implication of higher-order titanium enolates.

Scheme 3.3.2 Hypothetical Formation of Higher-Order TiCl_4 Enolates

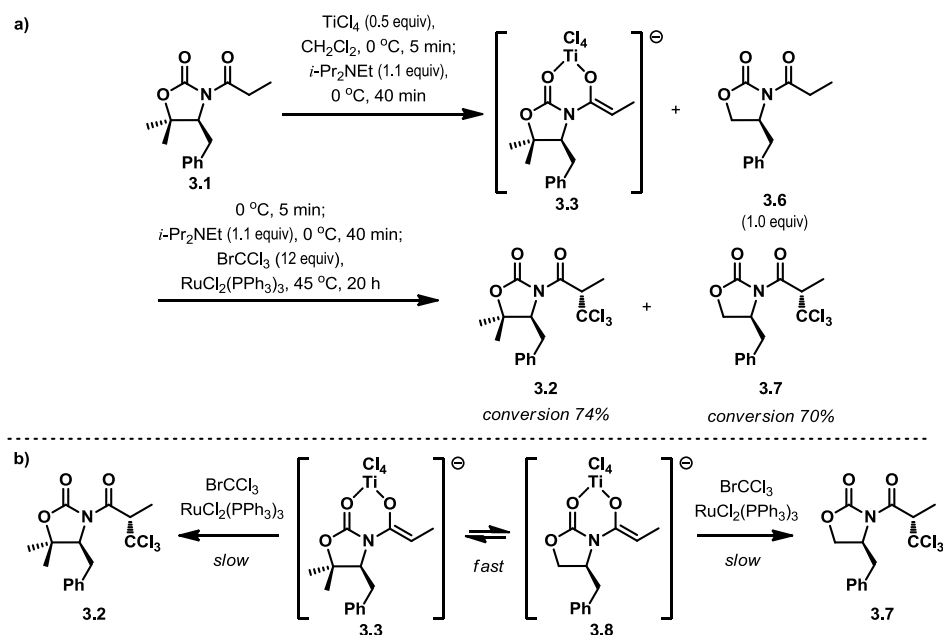


Higher-order enolates during the enolization of **3.1** with substoichiometric TiCl_4 . Bn=benzyl.

The next series of experiments was designed to probe the catalytic recovery of titanium tetrachloride. Specifically, we aimed to establish whether titanium tetrachloride could be efficiently transferred between different *N*-acyloxazolidinone species once enolization was completed. The cross-over experiment in Scheme 3.3.3³³ was particularly illuminating and revealed a number of notable factors. When the enolization of **3.1** was complete (TiCl_4 0.5

equiv), Hünig's base (1.1 equiv), 0 °C, 45 min), the *N*-acyloxazolidinone **3.6** (1.0 equiv) was added along with additional Hünig's base (1.1 equiv), and, after 40 min at 0 °C, the ruthenium-catalyzed radical trichloromethylation was initiated under the standard conditions. With the ultimate loading of titanium tetrachloride at 0.25 equivalents, products **3.2** and **3.7** resulting from the trichloromethylation of both substrates were produced in nearly equimolar amounts, which provided conclusive support for a rapid transfer of TiCl₄ between different *N*-acyloxazolidinone species in the presence of diisopropylethylamine. This experiment corroborates the feasibility of the catalytic turnover of TiCl₄ and suggests inhibition by the amine as a reason for its poor efficiency. It can be hypothesized that a fast equilibrium is established between titanium enolates **3.3** and **3.8** (Scheme 3.3.3b). This process is accompanied by a slow radical addition, and the distribution of products **3.2** and **3.7** is determined by the Curtin–Hammett principle.

Scheme 3.3.3 Cross-over Experiment



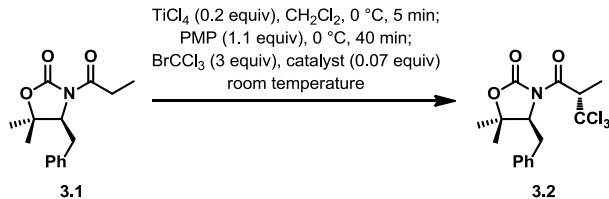
a) Cross-over experiment; b) product distribution is in accord with the Curtin–Hammett principle.

To ascertain the influence of the amine on the efficiency of the catalytic turnover of titanium tetrachloride and to probe further the equilibrium in Scheme 3.3.1b, we carried out the trichloromethylation reaction with various amounts of the Hünig's base as well as less-hindered triethylamine and more-hindered 1,2,2,6,6-pentamethylpiperidine (PMP; Table 3.3.1). An increase in the concentration of the Hünig's base consistently resulted in lower conversion (Table 3.3.1, entries 5 and 6), which supports the proposed inhibitory effect of the amine.

Remarkably, both less-hindered triethylamine and more-hindered PMP proved to be superior to the Hünig base for the catalytic turnover of TiCl_4 . Complete conversion was observed with 30 mol % of TiCl_4 with 3 equivalents of Et_3N , whereas conversion was 76 % with 1.1 equivalents of the amine (Table 3.3.1, entries 7 and 8). The same conversion (ca. 75 %) was observed with 10 mol % of TiCl_4 and Et_3N (3 equiv). Interestingly, no inhibitory effect was observed for triethylamine. With PMP (1.1 equiv), full conversion was observed with either 10 or 30 mol % of TiCl_4 (Table 3.3.1, entries 12 and 13). As with Et_3N , no inhibition of the trichloromethylation reaction was observed in the presence of excess PMP. Thus, the inhibitory effect appears to be confined to the Hünig's base.

We compared the original catalyst, $[\text{RuCl}_2(\text{PPh}_3)_3]$, with a more active catalyst, $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$,⁸⁴ to ascertain whether the rate of trichloromethylation was limited by low catalytic turnover frequency of TiCl_4 or other factors associated with the radical process (Scheme 3.3.4). When the reaction was carried out at room temperature in the presence of TiCl_4 (20 mol %) and PMP (1.1 equiv), a substantial acceleration of the process was observed with $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$ as the redox catalyst. This observation indicates that radical generation is the rate-limiting step, and both the turnover frequency of TiCl_4 and the addition of $\cdot\text{CCl}_3$ to the titanium enolate are relatively fast (Scheme 3.3.3b).

Scheme 3.3.4 Catalysis Comparison

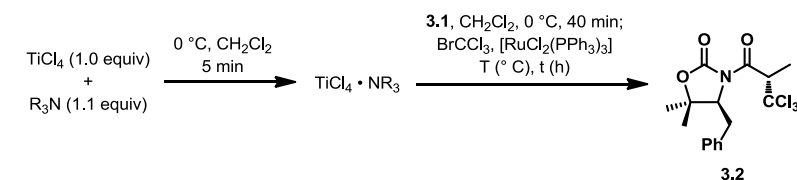


Catalyst	<i>t</i> (h)	Conversion (%)
$[\text{RuCl}_2(\text{PPh}_3)_3]$	48	76
$[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$	3	93

Comparison between $[\text{RuCl}_2(\text{PPh}_3)_3]$ and $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$ as the redox catalyst for radical generation. $\text{Cp}^*=1,2,3,4,5\text{-pentamethylcyclopentadienyl anion}$.

In the next series of experiments, the order of reagent addition during the formation of the titanium enolate was changed to examine the irreversibility of the formation of TiCl_4 –amine complexes under the trichloromethylation reaction conditions. The seminal studies by Evans et al. emphasized the importance of the initial TiCl_4 –substrate complexation; no enolate formation was observed if diisopropylethylamine or triethylamine were allowed to react with uncomplexed titanium tetrachloride first.⁴⁵ Therefore, we were surprised to discover substantial conversion in experiments in which TiCl_4 and the amine were mixed prior to the addition of the substrate (Table 3.3.2). Although the conversion was lower than that observed under the original enolization conditions, these results indicate notable, albeit rather inefficient, reversibility in the formation of TiCl_4 –amine adducts.

Table 3.3.2 Influence of the Inverse Addition of the Amines on Conversion.



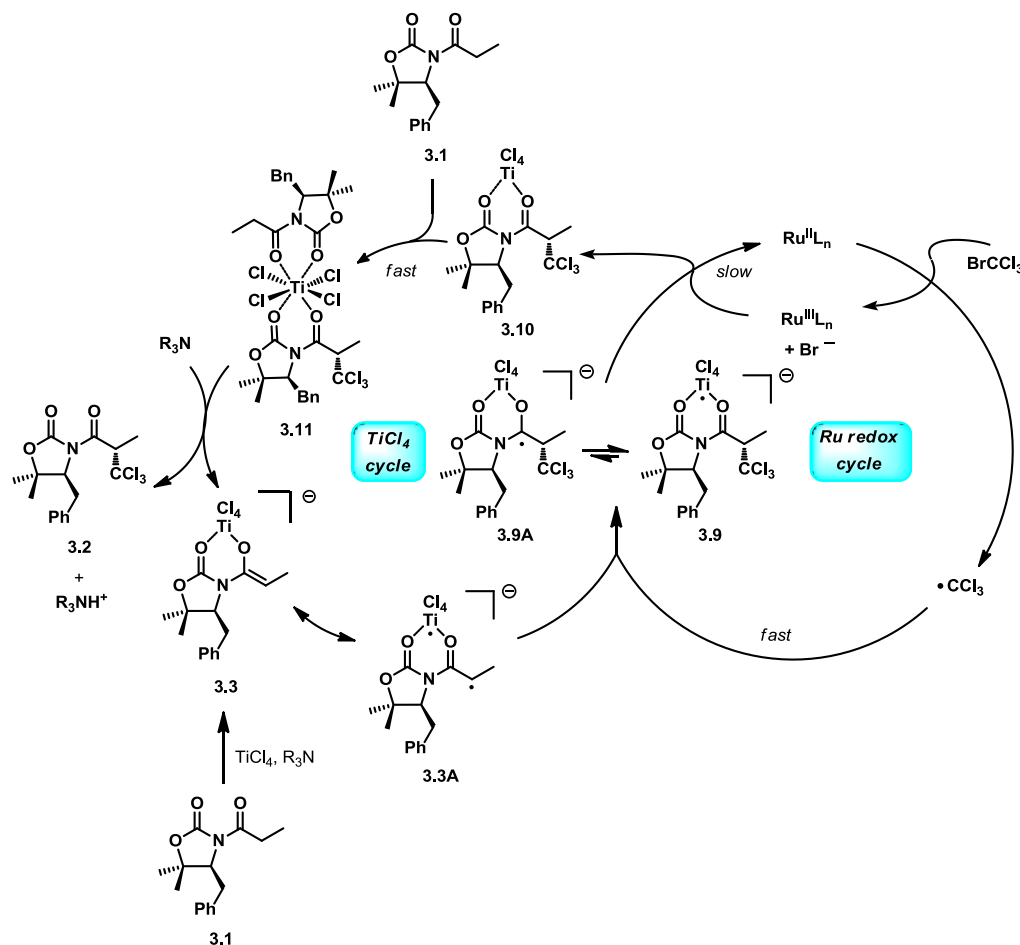
Entry	Amine (equiv)	T (° C)	t (h)	Conversion (%)
1	<i>i</i> Pr ₂ NEt	20	12	41
2	<i>i</i> Pr ₂ NEt	45	12	45
3	<i>i</i> Pr ₂ NEt	50	24	57
4	PMP	20	12	57
5	PMP	45	12	63
6	Et ₃ N	45	12	35

(a) Conversion was determined by ¹H NMR spectroscopy of the crude mixture of products. (b) The reaction time was 48 h. PMP = 1,2,2,6,6-pentamethylpiperidine.

On the basis of the experimental results of this study, we propose the catalytic cycle depicted in Scheme 3.3.5 for the dual Ru–Ti catalysis in the direct trichloroalkylation of *N*-acyl oxazolidinones. An initial complexation of TiCl₄ and substrate **1**, followed by addition of the amine, produces enolate **3.3** along with its biradical valence tautomer **3.3A**.^{79,85} An electron transfer from the Ru^{II} catalyst to BrCCl₃ generates ·CCl₃, which adds to the electron-rich titanium enolate to directly afford **3.9**, rather than the carbon-centered radical **3.9A**, along with the Ru^{III} counterpart.⁸⁶ Intermediate **3.9**, which is essentially the final product **3.2** complexed to a Ti^{III} center, regenerates the Ru^{II} catalyst, by a slow, rate-limiting single-electron-transfer event, to give the Ti^{IV} chelate **3.10**. At this stage, TiCl₄ is transferred directly and at a relatively high rate to another molecule of the substrate, potentially via an octacoordinated species, such as **3.11**. Alternatively, TiCl₄ can be intercepted by excess

amine, which accounts for the inhibitory effect of the amine. It is highly unlikely that uncoordinated TiCl_4 is present at any time during the course of the reaction.⁸⁷

Scheme 3.3.5 Proposed Mechanism for Ti-Ru Catalysis in the Radical Haloalkylation of Titanium Enolates.



In summary, a direct radical trichloromethylation reaction that is catalytic in both the titanium and ruthenium reagents has been developed as a result of a deeper mechanistic investigation of the process. This reaction constitutes the first alkylation of titanium enolates that is catalytic in titanium and provides a foundation for expanding the scope of catalytic radical alkylation reactions of titanium enolates. Important findings include: 1) the discovery that the complexation of trialkyl amines to TiCl_4 appears to be reversible, especially at

elevated temperatures, although the decomplexation is of limited efficiency; and 2) the observation that the turnover frequency for the catalytic transfer of TiCl_4 is relatively high in comparison with the rate of radical generation, even with the more reactive ruthenium catalyst $[\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2]$.

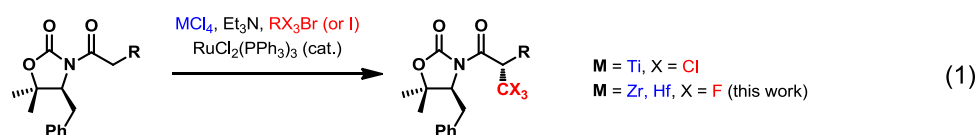
3-4 Asymmetric Trifluoromethylation of *N*-Acyl Oxazolidinones via Ru-Catalyzed Radical Addition to Zirconium Enolates

3-4-1 Initial Trifluoroalkylation Studies

The growing appreciation of unique physical and chemical properties of fluorinated organic compounds has resulted in their increasingly broad application in medicine, materials sciences, agrochemicals, and many other areas of research.⁸⁸ In order to enable future advances in the discovery and application of fluorinated materials, practical methods for efficient and selective fluorination are needed. Within this general context,^{88a,89} stereoselective introduction of the trifluoromethyl and other perfluoroalkyl groups at the α -position of carbonyl compounds has remained an ongoing challenge, with several notable developments reported in the past few years. Following early studies in diastereoselective radical trifluoromethylation of lithium enolates employing the iodotrifluoromethane–Et₃B/O₂ system for CF₃ radical generation,⁹⁰ a number of elegant alternatives based on electrophilic,⁹¹ radical,⁹² or photoredox organocatalytic strategies⁹³ have been developed.⁹⁴ These methods collectively constitute important advances toward highly selective α -fluoroalkylation of a diverse range of carbonyl compounds and highlight novel patterns of reactivity. On the other hand, issues of practicality related to experimental simplicity, cost of reagents, and energy efficiency (use of cryogenic conditions or high temperatures) remain persistent, stimulating continued progress in this area.

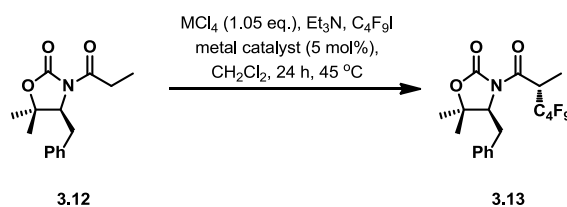
After, we demonstrated that an experimentally simple, high-yielding diastereoselective α -trichloromethylation of titanium enolates can be achieved.⁹⁵ The process is based on a Ru-catalyzed redox formation of the trichloromethyl radical from BrCCl₃ followed by its

addition to catalytically generated titanium enolates derived from chiral *N*-acyl oxazolidinones. This type of radical addition may be facilitated by the putative biradical character of titanium enolates.⁹⁶ Overall, the process allows for a direct, one-step chloroalkylation of *N*-acyl oxazolidinones, and its utility in the synthesis of natural products with CCl₃-substituted stereogenic centers has been highlighted.^{95c,97} Although direct extension of this type of reactivity to fluoroalkylation reactions has proven to be highly challenging, we have succeeded in reaching this goal by enlisting in situ generated zirconium enolates (eq 1). The development of this protocol highlighting operational simplicity in the direct α -fluoroalkylation of *N*-acyl oxazolidinones is described herein.⁹⁸



Early attempts to extend the chloroalkylation reaction of titanium enolates to fluoroalkylations concentrated on screening a range of transition metal catalysts, including those that have been previously used in Kharasch-type additions of iodoperfluoroalkanes to olefins. Typical examples include [Ph₃P]₃RuCl₂,⁹⁹ Ru₃(CO)₁₂,¹⁰⁰ Fe₃(CO)₁₂,¹³ and Co₂(CO)₈,¹³ however, in no instance any amount of fluoroalkylation product was detected. After exhausting our options with titanium enolates, we explored other metal halides potentially capable of effecting soft enolizations (SmBr₃, BiCl₃, InCl₃, Yb(OTf)₃, VOCl₃, VCl₃, VCl₄, ZrCl₄, HfCl₄).¹⁰¹ In contrast to our expectations, it was the group IVa metal halides, ZrCl₄ and HfCl₄,¹⁰² that proved to be uniquely competent in the fluoroalkylation reactions.

Table 3.4.1 Identification of Transition Metal Catalysts Suitable for Fluoroalkylation of Zirconium and Hafnium Enolates^a.



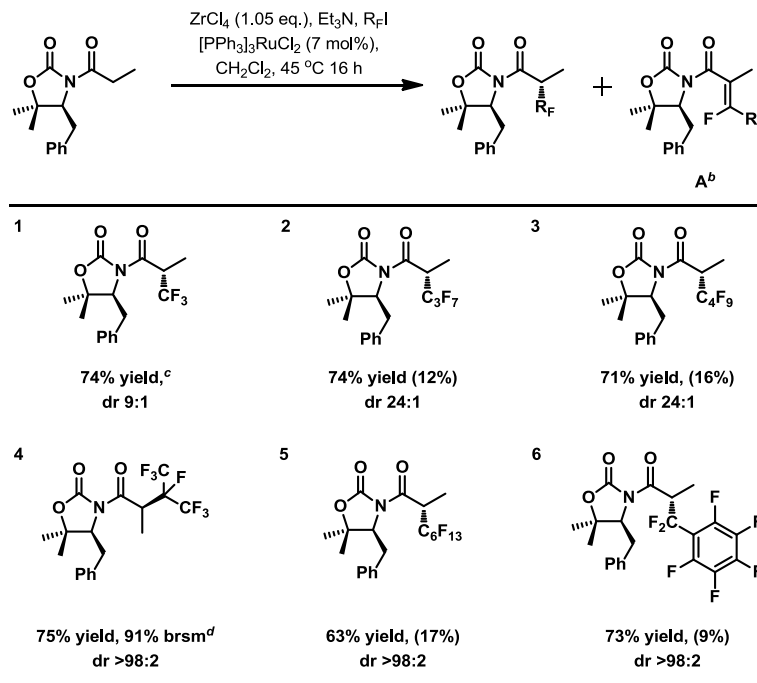
Entry	MCl_4	metal catalyst (5-7 mol %)	Conversion ^b (%)	3.13 (%) ^b
1	ZrCl_4	$\text{Fe}_3(\text{CO})_{12}$	17	0
2		$\text{Co}_2(\text{CO})_8$	26	0
3		$\text{Ru}_3(\text{CO})_{12}$	37	0
4		FeBr_2	31	0
5		$\text{Cu}(\text{OEP})^f$	33	0
6		$[\text{Rh}(\text{cod})\text{Cl}]_2$	30	0
7		$[(p\text{-cymene})\text{RuCl}_2]_2$	46	22
8		$[(\text{C}_6\text{H}_6)\text{RuCl}_2]_2$	61	28
9		$\text{IndRu}[\text{PPh}_3]_2\text{Cl}\cdot\text{CH}_2\text{Cl}_2$	49	19
10		$\text{Cp}^*\text{Ru}[\text{PPh}_3]_2\text{Cl}$	87	59 ^c
11 ^e		$\text{Ru}[\text{PPh}_3]_3\text{Cl}_2^g$	97	74 ^d
12 ^e	HfCl_4	$\text{Ru}[\text{PPh}_3]_3\text{Cl}_2^g$	>98	57

(a) Standard conditions: 1 (0.50 mmol), ZrCl_4 (1.05 equiv), Et_3N (2.0 equiv), $n\text{-C}_4\text{F}_9\text{I}$ (5.0 equiv), CH_2Cl_2 (~0.1 M), mixed and stirred at 45 °C for 24 h. (b) Determined by the 500 MHz NMR analysis of the crude mixture of products. (c) In addition, 18% of α,β -unsaturated byproduct resulting from HF elimination has also been observed. (d) In addition, 12% of α,β -unsaturated byproduct resulting from HF elimination has also been observed. (e) $n\text{-C}_3\text{F}_7\text{I}$ (5.0 equiv) was used. (f) OEP = 2,3,7,8,12,13,17,18-octaethyl-21*H*,23*H*-porphyrine. (g) 7 mol % of the metal catalyst was used.

Once these metal halides had been identified, a number of transition metal redox catalysts for the generation of perfluoroalkyl radicals were examined (Table 3.4.1). Among these, ruthenium catalysts emerged as the most promising (entries 7–11), with Ru[Ph₃P]₃Cl₂, the catalyst used in the original chloroalkylation of titanium enolates, being the most effective. The ruthenium-catalyzed perfluoropropylation of *N*-acyl oxazolidinones **3.12**, which served as a benchmark reaction, was characterized by a clean transformation to **3.13** using only a moderate excess (5 equiv) of *n*-C₃F₇I (entry 11). The side products were comprised of only the α,β -unsaturated imide as a result of HF elimination from **3.13** (12%) and the cleaved oxazolidinone auxiliary (11%),¹⁰³ which together accounted for the majority of the remaining mass balance. Similar outcomes were observed with hafnium enolates derived in situ from hafnium tetrachloride and Et₃N (entry 12).

The scope of perfluoroalkylating agent was investigated next (Table 3.4.2).¹⁰⁴ No byproduct resulting from α,β -elimination of hydrogen fluoride was observed in any trifluoromethylation reactions (entry 1; also see Table 3.4.3). We did observe partial (9–17%) formation of an α,β -unsaturated byproduct (**A**) with primary perfluoroalkyl- and perfluorobenzyl-substituted products (entries 2, 3, 5, and 6). As in the trifluoromethylation reaction, no HF elimination was detected when the 2-perfluoropropyl group was introduced (entry 4).

Table 3.4.2 Scope of Perfluoroalkylating Agent^a



(a) Yields of isolated products are reported. The numbers in parentheses are yields of the corresponding α,β -unsaturated byproduct **A**, when observed. Diastereomer ratios were determined by 500 MHz ^1H NMR analysis.

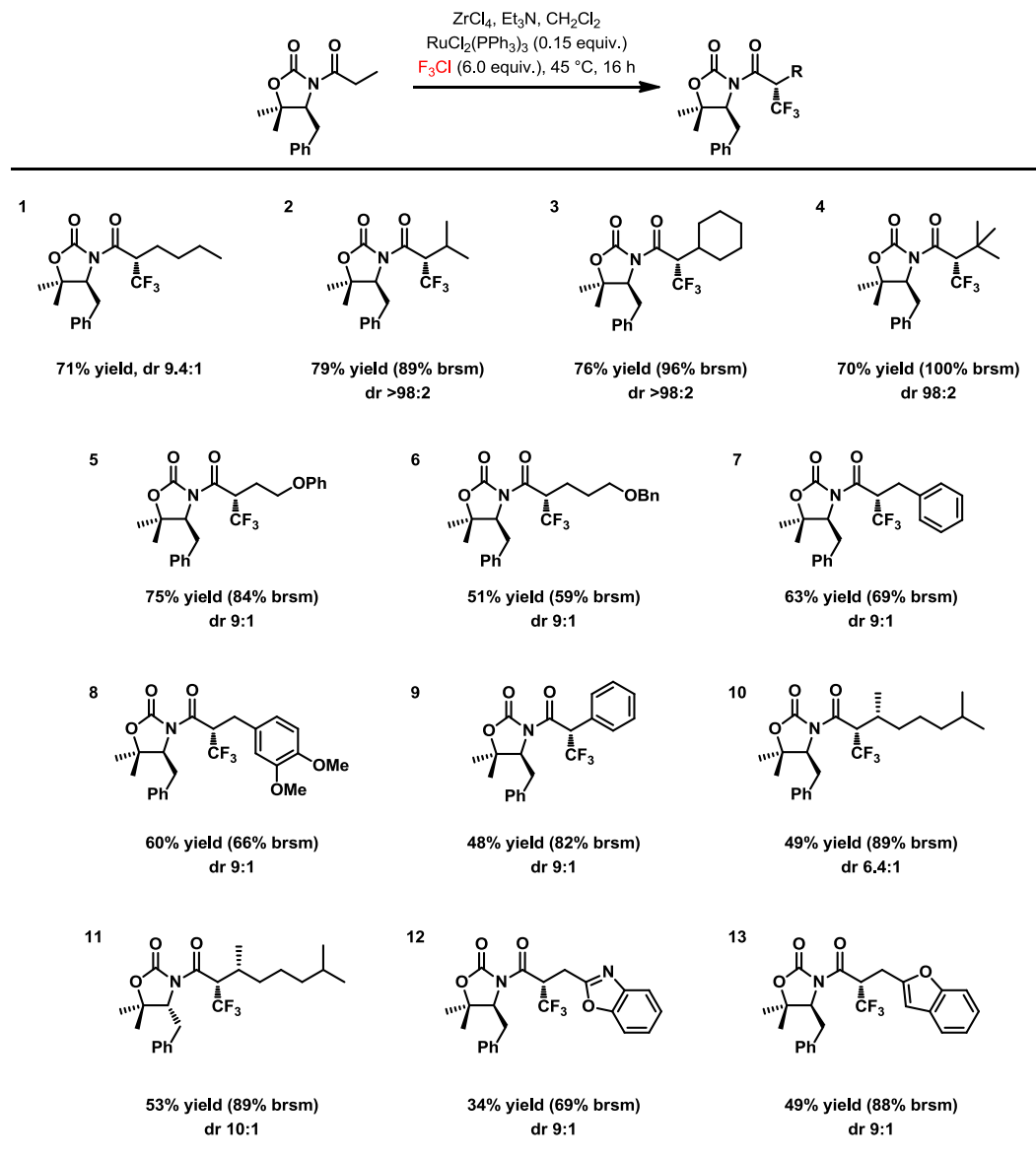
(b) observed for primary perfluoroalkyl groups only. (c) 15 mol % of $[\text{Ph}_3\text{P}]_3\text{RuCl}_2$ were used. (d) brsm = based on recovered starting material.

A variety of *N*-acyl oxazolidinones can be successfully trifluoromethylated using the simple protocol developed in the course of this investigation (Table 3.4.3). We found that reagents can be mixed all at once in any order at room temperature with no influence on the isolated yield of the desired product. Therefore, the reaction setup can be guided solely by experimental convenience rather than by other factors intrinsic to the reaction. *N*-Acyl oxazolidinones obtained from unfunctionalized alkanolic acids undergo efficient and diastereoselective trifluoromethylations, with yields increasing for β -branched substrates (entries 1–4). These are clean transformations, where unreacted starting material is the major byproduct as indicated by yields based on recovered starting materials (entries 2–4), while

auxiliary cleavage (25%) was observed for the reaction in entry 1. The presence of aryl and benzyl ethers is well-tolerated (entries 5, 6), as is the presence of functionalized β -aryl substitution, although the extent of chiral auxiliary detachment was higher (31–34% for entries 7, 8). Substitution with a phenyl group at the α -position resulted in a clean reaction (82% yield brsm, entry 9), albeit at a reduced conversion under the standard conditions (59%). Diastereoselective alkylations controlled by the oxazolidinone stereochemistry can be performed with substrates that have a stereogenic center at the β -position in the *N*-acyl substituent (entries 10, 11). More functionalized heterocyclic substituents such as benzofurans and benzoxazoles are also compatible with the reaction conditions (entries 12, 13).

The proposed mechanism of the reaction based on the related Ru-catalyzed trichloromethylation is depicted in Scheme 3.4.1.^{95a,97} NMR spectroscopic studies of the enolate formation using *N*-propionyl oxazolidinones **3.12**, zirconium tetrachloride, triethylamine, and CDCl₃ revealed that a rapid, clean, and essentially complete enolization producing enolate **3.15** occurs at room temperature. We succeeded in obtaining a single-crystal X-ray structure of a complex between the substrate and ZrCl₄ revealing a nearly perfectly planar arrangement of atoms in the six-membered cyclic chelate **3.17** which is in all respects similar to the corresponding titanium complex (not shown). Therefore, we surmise that the geometric structures of the zirconium (**3.15**) and titanium enolates are similar, and it is the dissimilarities in their electronic structure that are responsible for differences in their reactivity in the ruthenium-catalyzed fluoroalkylation reaction. Once **3.15** is formed, it undergoes an addition reaction with the trifluoromethyl radical generated by a

Table 3.4.3 Scope of *N*-Acyl Oxazolidinones in the Trifluoromethylation Reaction^a

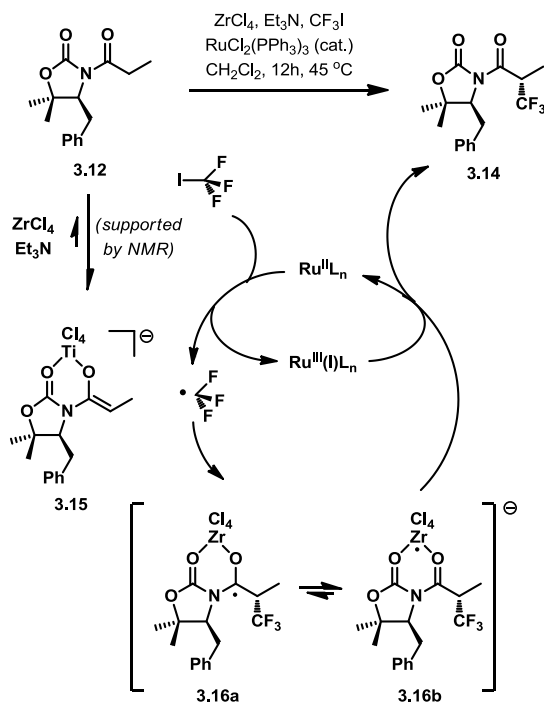


(a) Yields of isolated products are reported. At least two experiments were carried out to confirm reproducibility. The numbers in parentheses are yields based on recovered starting material (brsm). Diastereomer ratios were determined by 500 MHz ¹H NMR analysis of the crude mixture of products.

redox process from iodotrifluoromethane and the ruthenium(II) catalyst. The addition product is probably better represented by resonance form **3.16b** rather than carbon-centered form **3.16a**, and a potential biradical character of **3.15** may facilitate the addition of the CF₃

radical. The ruthenium catalyst is recovered by a single electron transfer from intermediate **3.16b** to Ru(III) species.

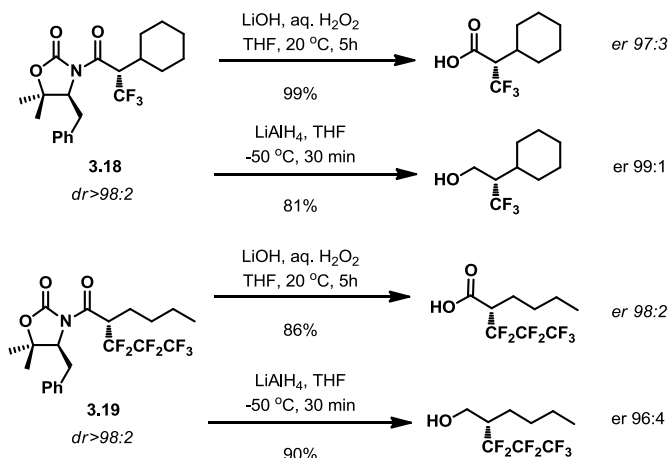
Scheme 3.4.1 Proposed Mechanism of the Ru-Catalyzed Trifluoromethylation Reaction



Additional insight into the course of the perfluoroalkylation was acquired from the following experiments. First, when the catalyst loading in the perfluoropropylation of **3.12** was increased from 7 to 30 mol %, the rate of the process was notably enhanced. The reaction was complete in 4 rather than 16 h, showing a substantially reduced level of side reactions and giving the expected product in 86% isolated yield. Similar, albeit somewhat lower efficiency was observed when the amount of $n\text{-C}_3\text{F}_7\text{I}$ was increased from 5 to 15 equiv. Taken together, these observations suggest that the generation of the perfluoroalkyl radical is the rate-limiting step of the process. Second, monitoring the course of the reaction performed in CD_2Cl_2 by ^1H and ^{19}F NMR spectroscopy revealed that another major pathway of reactivity for $n\text{-C}_3\text{F}_7\text{I}$ is reduction to $n\text{-C}_3\text{F}_7\text{H}$, which presumably occurs by oxidation of

triethylamine. Overall, these key observations are expected to aid in developing more efficient perfluoroalkylation processes based on radical additions to transition metal enolates.

Scheme 3.4.2 Preparation of Versatile Enantioenriched Fluorinated Building Blocks by Hydrolytic and Reductive Removal of the Chiral Auxiliary^a



(a) The chiral auxiliary is recovered in nearly quantitative yield in all reactions.

Conversion of the reaction products to broadly useful fluorinated building blocks for organic synthesis is illustrated by examples in Scheme 3.4.2 that include hydrolytic and reductive removal of the chiral auxiliary. Trifluoromethyl-substituted derivative **3.18** and perfluoropropyl derivative **3.19**¹⁰⁵ could be readily hydrolyzed with a LiOH–H₂O₂ reagent system to the corresponding carboxylic acids with a high level of retention of stereochemical integrity. While reductions of these compounds with sodium borohydride in aqueous THF were sluggish, removal of the oxazolidinone could be readily achieved by treatment with lithium aluminum hydride. For substrate **3.19**, virtually complete preservation of stereochemistry was observed, while only a minor erosion of stereochemistry was noted for

the perfluoropropyl-substituted substrate. Notably, these transformations are characterized by very good yields and nearly quantitative recovery of the chiral auxiliary.

In closing, we report an experimentally simple asymmetric fluoroalkylation reaction of *N*-acyl oxazolidinones based on the unique radical reactivity of group IVa metal enolates. For titanium enolates, the biradical character has been supported by computational and spectroscopic studies that provide an intriguing conceptual basis for reaction development. From a practical perspective, the reaction requires inexpensive reagents, which can be mixed in any order, and mild heating over the course of a few hours delivers fluoroalkylation products directly in good yields and high diastereoselectivities. Ongoing studies are directed at the development of a more active catalytic system, catalytic generation of the metal enolate, and defining a more detailed picture for the mechanism of the reaction.

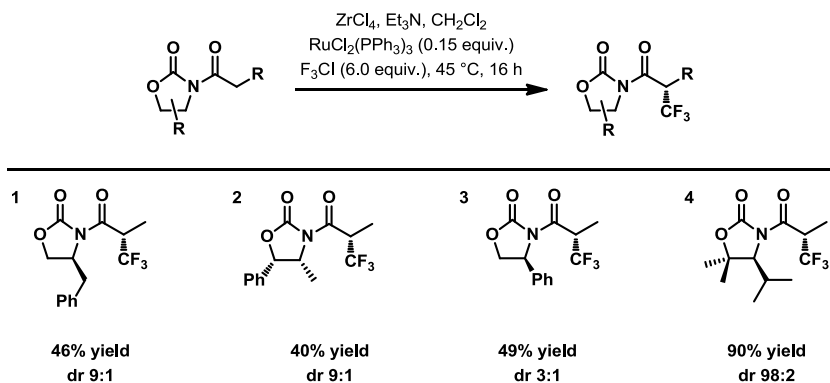
3-4-2: Continuing Trifluoroalkylation Studies

After the preliminary trifluoroalkylation studies, further investigations were conducted to increase either yield or diastereoselectivity. An initial screen of oxazolidinones was conducted to see the effect on diastereoselectivity as seen in Table 3.4.3. We found that if there was a lack of quaternary substitution at the 5-position on the auxiliary; it led to low yield and decomposition of the starting material (entries 1-3). Further screening indicated that an isopropyl auxiliary led to improvement for yield and diastereoselectivity (entry 4).

After selecting 4-isopropyl-5,5-dimethyloxazolidin-2-one as the auxiliary, a small screen of *N*-acyl oxazolidinones was conducted as shown in Table 3.4.4. For all substrates both catalyst loading and reaction time was decreased by 50% or more. Drastic improvement in both yield +19% and diastereoselectivity >98:2 was observed for the *N*-Acyl oxazolidinones obtained from hexanoic acid (Table 3.4.4, entry 1). An astonishing increase in yield (+30%)

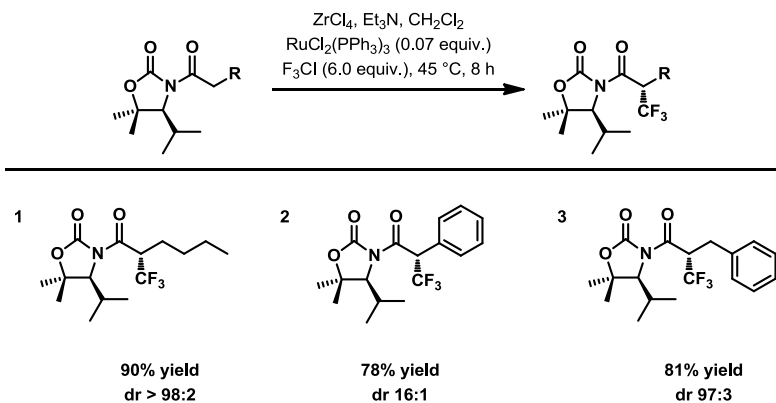
and slight improvement in diastereoselectivity was observed for phenyl acetic acid derivative (entry 2).

Table 3.4.3 Scope of *N*-Acyl Oxazolidinones in the Trifluoromethylation Reaction^a



(a) Yields of isolated products are reported. Diastereomer ratios were determined by 500 MHz ¹H NMR analysis.

Table 3.4.4 Scope of Trifluoromethylation of Isopropyl *N*-Acyl Oxazolidinone^a



(a) Yields of isolated products are reported. Diastereomer ratios were determined by 500 MHz ¹H NMR analysis.

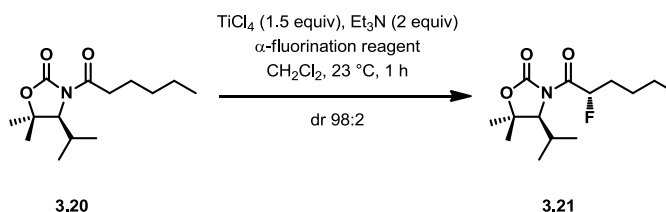
3.5 Stereoselective α -Fluorination of *N*-Acyl Oxazolidinones at Room Temperature

The importance of organofluorine compounds has been amply validated by broad application in medicinal sciences, materials, and agrochemicals.¹⁰⁶ Fluorine incorporation is typically performed to acquire the unique physical and chemical properties that fluorine substitution imparts on organic compounds. Although many methods for fluorination have already been reported in the literature,^{106a,106b,106m,107} future advancements in the discovery and application of fluorinated materials require the availability of new methods for economical and selective fluorination. Despite the broad utility of fluorine-containing organic compounds, stereoselective incorporation of the fluorine atom at the α -position of the carbonyl group has remained an ongoing challenge; several notable recent developments exploit reagent, catalyst, or substrate control in α -fluorination reactions.¹⁰⁸ Following early work on diastereoselective electrophilic α -fluorination of lithium enolates with *N*-fluoro-*o*-benzenedisulfonimide (NFOBS) as the fluorinating reagent,¹⁰⁹ a number of elegant alternatives describing the use of *N*-fluoropyridinium 2,8-diazobicyclo[2,2,2]octane and sulfonamide reagents as the electrophilic source of fluorine were developed.¹¹⁰ In all, these methods expanded the repertoire of selective α -monofluorination for a diverse range of carbonyl compounds, at the same time highlighting their unique patterns of reactivity. On the other hand, issues of practicality, limitations in substrate scope, high cost of reagents, extended reaction time, and energy efficiency (use of cryogenic conditions or high temperatures) remain persistent, stimulating continued progress in this area.

Demonstration of the efficacy of group IVa metal enolates generated by soft enolization¹¹¹ in ruthenium-catalyzed radical trichloromethylation, trifluoromethylation, and perfluoroalkylation reactions.¹¹² We applied this experimentally simple protocol, good to

high yields of various α -haloalkylation products can be achieved with high diastereoselectivity. Herein, we describe the utility of group IVa metal enolates derived from *N*-acyl oxazolidinones in rapid economical and operationally simple electrophilic α -fluorination reactions that take place at room temperature and display high diastereoselectivity.

Table 3.5.1 Identification of Optimal Fluorinating Reagent^a



Entry	Reagent	Conversion ^b (%)	\$/mmol
1	NFSI	99	\$0.35 ^c
2	Selectfluor	70 ^d	\$0.82 ^e
3	1-fluoro-2,4,6-trimethylpyridinium triflate	<1	\$3.67 ^f
4	1-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate	<1	\$4.09 ^f

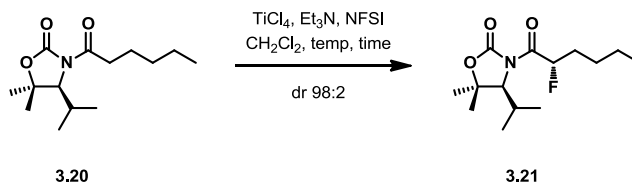
(a) Standard conditions: **3.20** (0.50 mmol), TiCl_4 (1.5 equiv), Et_3N (2.0 equiv), CH_2Cl_2 (0.5 M), reagent (2.0 equiv), mixed and stirred at room temperature for 1 h. (b) Determined by the 600 MHz NMR analysis of the crude mixture of products. (c) Oakwood Products. (d) Reaction solvent was a 1:1 mixture of acetonitrile/ CH_2Cl_2 , dr 5:1. (e) Apollo Scientific. (f) TCI America.

The aim of initial experiments was to identify the optimal electrophilic source of fluorine, with the chemical efficiency of the α -fluorination reaction and reagent cost being the most important factors (Table 3.5.1). Examination of the most common commercial sources of electrophilic fluorine, summarized in Table 3.5.1, revealed that *N*-fluorobenzenesulfonimide (NFSI), the most inexpensive reagent tested, displayed superior

performance by a substantial margin. Under standard conditions, complete conversion in the α -fluorination of **3.20** was achieved with NFSI within 1 h at room temperature. The reaction occurred with a diastereoselectivity of 98:2. Selectfluor, the second best reagent, provided 70% conversion with a decrease of diastereoselectivity to 5:1, whereas both 1-fluoro-2,4,6-trimethylpyridinium triflate and 1-fluoro-2,4,6-trimethylpyridinium tetrafluoroborate were not efficient sources of electrophilic fluorine due to lack of solubility in dichloromethane.

Early experimentation also revealed a rather high reactivity of titanium enolates in the α -fluorination reaction. In contrast to other reported stereoselective α -fluorinations of carbonyl compounds, the reaction reaches 90% conversion within 30 min at room temperature while maintaining high diastereoselectivity (Table 3.5.2, entry 1). Full conversion requires 60 min at 23 °C (Table 3.5.2, entry 2). Under optimized conditions, 1.5 equiv of TiCl_4 and 2 equiv each of Et_3N and NFSI are required for full conversion (Table 3.5.2, entry 5), and reduction in the stoichiometry of any of these reagents erodes conversion (Table 3.5.2, entries 4 and 6–9) with the strongest effect observed for NFSI (Table 3.5.2, entry 4).¹¹³ Similar results, including high diastereoselectivity of 98:2, were noted when ZrCl_4 and HfCl_4 (Table 3.5.2, entries 10 and 11) were used for enolate generation under identical conditions, although conversions were lower by about 10%.¹¹⁴ All three common oxazolidinones surveyed 3-propionyl-5,5-dimethyl-4-benzyl- (Table 3.5.2, entry 12), 3-propionyl-5,5-dimethyl-4-isopropyl-, and 3-propionyl-4-benzyloxazolidin-2-ones (Table 3.5.2, entry 13) showed high diastereoselectivity (>10:1), with the 5,5-dimethyl-4-isopropyl derivative related to **3.20** giving the highest stereoselectivity (dr 98:2). Therefore, further studies were carried out with NFSI as the fluorinating reagent and the 5,5-dimethyl-4-isopropyl-substituted oxazolidinone as the stereodirecting group.

Table 3.5.2 Optimization of α -Fluorination Reaction^a



Entry	TiCl ₄ (equiv)	Et ₃ N (equiv)	NFSI (equiv)	Time (h)	Conversion ^b (%)
1	2.0	3.0	2.0	0.5	90
2	2.0	3.0	2.0	1	99
3	2.0	2.0	2.0	1	99
4	2.0	3.0	1.25	1	50
5	1.5	2.0	2.0	1	99
6	1.25	2.0	2.0	1	93
7	1.5	1.5	1.5	1	77
8	0.5	3.0	2.0	12	40 ^c
9	1.0	3.0	2.0	12	80 ^c
10	1.5 (ZrCl ₄) ^d	2.0	2.0	1	87
11	1.5 (HfCl ₄) ^e	2.0	2.0	1	78
12	1.5	2.0	2.0	1	99 ^f

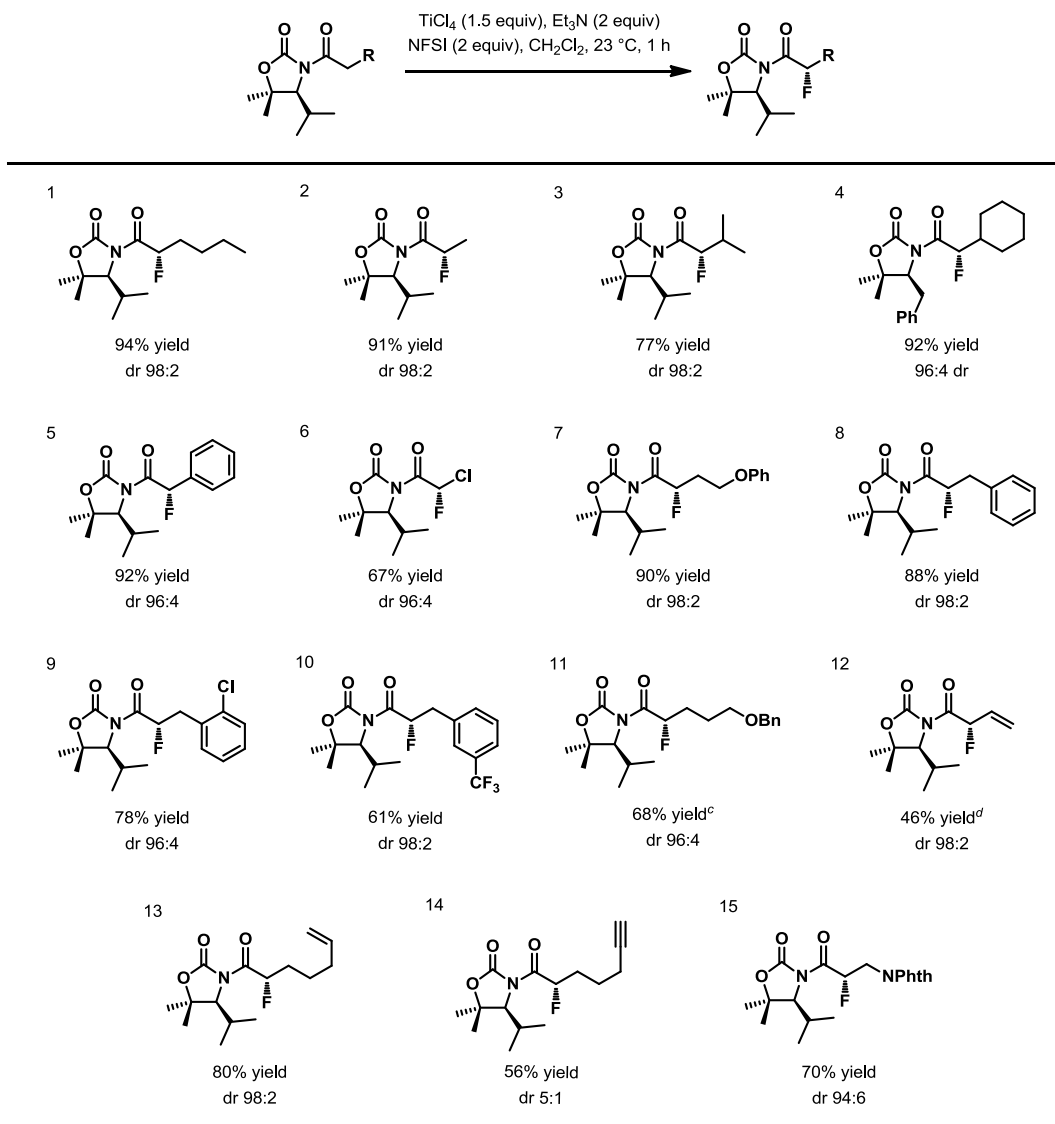
(a) Standard conditions: **3.20** (0.50 mmol), CH₂Cl₂ (0.5 M), mixed and stirred at room temperature. (b) Determined by the 600 MHz ¹H NMR analysis of the crude mixture of products. (c) Reactions were performed at 45 °C. (d) ZrCl₄ was used in place of TiCl₄. (e) HfCl₄ was used in place of TiCl₄. (f) 3-propionyl-5,5-dimethyl-4-benzyl-2-oxazolidin-2-one was used (dr 96:4).

Substrates derived from simple unfunctionalized alkanoic acids generally afford high yields of α -fluorination products with high diastereoselectivity under standard conditions at room temperature within 1 h (Table 3.5.3, entries 1-4). The derivative of isovaleric acid (Table 3.5.3, entry 3) afforded a somewhat depressed yield of 77% due to competitive formation of α -chlorination product (10% yield, >99:1 dr). 3-Phenylacetyl-5,5-dimethyl-4-

isopropylloxazolidinone afforded the α -fluorination product in high yield and diastereoselectivity (Table 3.5.3, entry 5). A unique derivative of α -chloro- α -fluoroacetic acid has been prepared by this procedure with high stereoselectivity (Table 3.5.3, entry 6). An example, entry 4, illustrates that analogues in which the stereodirecting 4-isopropyl substituent is replaced with a benzyl group provide comparable yields and diastereomeric ratios of α -fluorination products. Aryl ether groups are well tolerated (Table 3.5.3, entry 7). A number of compounds produced from hydrocinnamic acids are also good substrates for the α -fluorination reaction (Table 3.5.3, entries 8-10), while benzyl ethers undergo partial debenzylation, which can be mitigated by replacing TiCl_4 with ZrCl_4 (Table 3.5.3, entry 11).

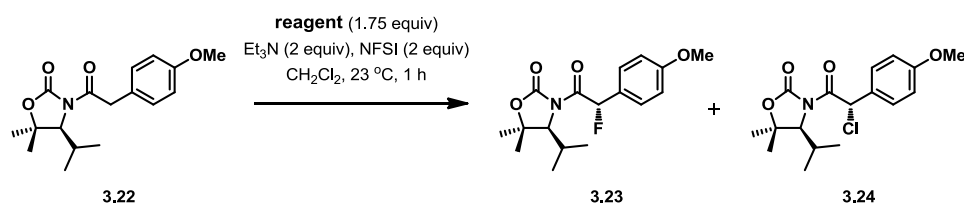
α -Fluorination via titanium enolates of substrates containing unsaturation can be accomplished efficiently in the presence of double bonds (Table 3.5.3, entries 12-13), yet terminal alkynes can display notably lower yields (Table 3.5.3, entry 14). Although no specific byproducts have presently been isolated, the lower efficiency can hypothetically be ascribed to the competitive formation of alkynyltitanium species under the reaction conditions. The protected form of α -fluoro- β -alanine can be prepared in 70% yield and 94:6 diastereomeric ratio (Table 3.5.3, entry 15). In most cases, the product can be isolated as the isomerically pure diastereomer either by recrystallization or flash column chromatography.

Table 3.5.3 Scope of *N*-Acyl Oxazolidinones in the α -Fluorination Reaction^{a,b}



(a) Standard conditions: substrate (0.50 mmol), TiCl_4 (1.5 equiv), Et_3N (2.0 equiv), NFSI (2.0 equiv), CH_2Cl_2 (0.5 M), mixed and stirred at room temperature for 1 h. (b) Yields of isolated products are reported. Diastereomer ratios were determined by 600 MHz ^1H NMR analysis of the crude mixture of products. (c) 1.5 equiv of ZrCl_4 was used in place of TiCl_4 . (d) (*S*)-3-(2-Butenoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one was used as the starting material.

Table 3.5.4 Optimization of α -Fluorination of 3-(4-Methoxyphenylacetyl)-5,5-dimethyl-4-isopropylloxazolidin-2-one **3.22**^{a,b}



Entry	Reagent	% 3.23 (dr) ^{b,c}	% 3.24 (dr) ^{b,c}
1	TiCl ₄	0	82 (1:1)
2	Ti(OPr- <i>i</i>) ₂ Cl ₂	52 (93:7)	41 (1:1)
3	Ti(OPr- <i>i</i>) ₂ Cl ₂ ·2E ₃ NHCl	77 (93:7)	17 (1:1)
4	Ti(OPr- <i>i</i>) ₃ Cl ₂ ·3E ₃ NHCl	17 (93:7)	0
5	Ti(OPr- <i>i</i>) Cl ₂ ·E ₃ NHCl	0	100 (1:1)
6	ZrCl ₄	0	100 (1:1)

(a) Standard conditions: **3.22** (0.50 mmol), Ti reagent (1.75 equiv), Et₃N (2.0 equiv), NFSI (2.0 equiv), CH₂Cl₂ (0.5 M), mixed and stirred at room temperature for 1 h. (b) Percent composition of the compound in the crude mixture of products as determined by 600 ¹H NMR analysis. (c) Diastereomeric ratio (dr) was determined by the 600 MHz ¹H NMR analysis of the crude mixture of products.

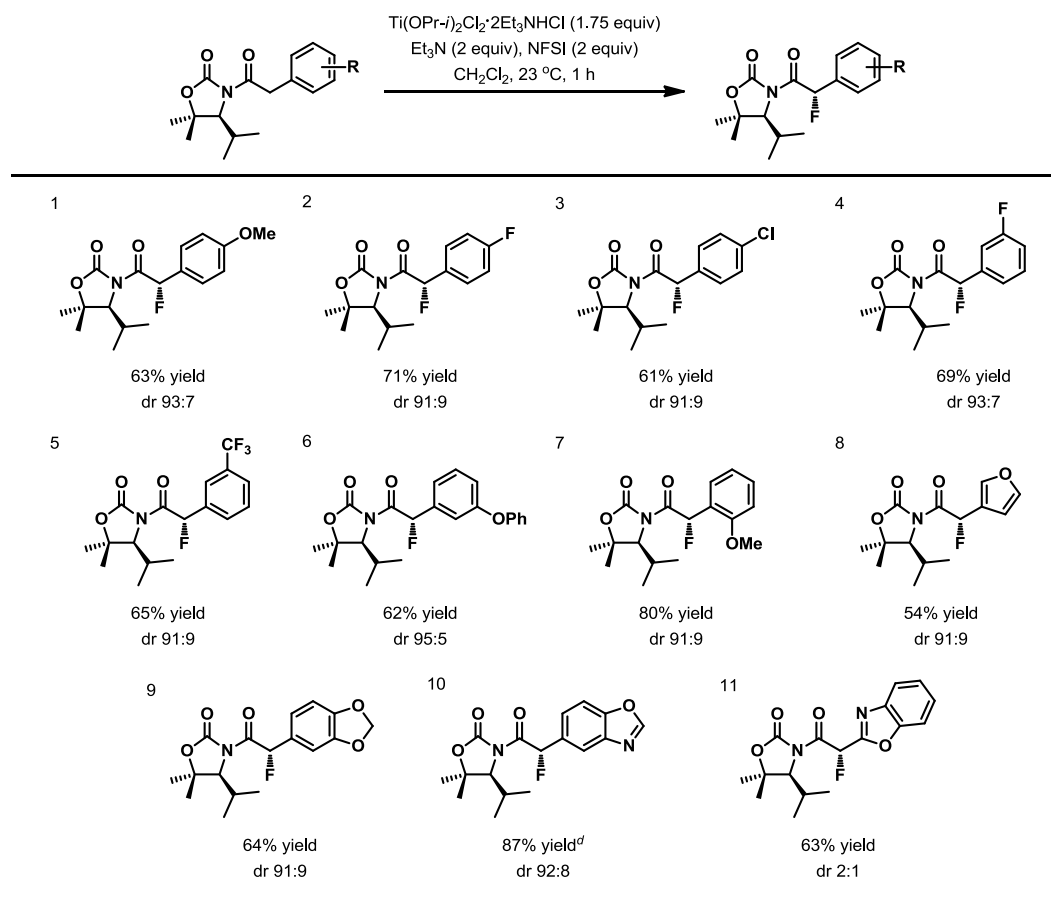
In contrast to the unfunctionalized phenylacetic acid derivative (cf. Table 3.5.4, **3.22**), substitution in the phenyl ring resulted in substantially different reactivity under the standard conditions. In fact, the attempted α -fluorination of 4-methoxyphenyl analogue **3.22** resulted in the exclusive formation of α -chlorination product **3.24** as a 1:1 mixture of diastereomers (Table 3.5.4, entry 1). The hypothesis that replacing TiCl₄ with an alternative titanium(IV) Lewis acid would minimize the competitive chlorination was put to the test next. Delightfully, a significant improvement in α -fluorination was achieved when Ti(OPr-*i*)₂Cl₂, prepared by a reaction of equimolar amounts of TiCl₄ and Ti(OPr-*i*)₄,¹¹⁵ was used for enolate

generation (Table 3.5.4, entry 2). When diisopropoxytitanium dichloride was prepared by an alternative procedure from TiCl_4 , 2 equiv of 2-propanol, and 2 equiv of triethylamine, a further improvement was achieved (Table 3.5.4, entry 3).¹¹⁶ The use of triisopropoxytitanium chloride, isopropoxytitanium trichloride, or zirconium tetrachloride led to either low reactivity or exclusive formation of the α -chlorination product (Table 3.5.4, entries 4–6).

With the protocol utilizing the $\text{Ti}(\text{OPr-}i)_2\text{Cl}_2 \cdot 2\text{Et}_3\text{NHCl}$ reagent, a range of substituted phenylacetic acid derivatives can be effectively α -fluorinated with very good diastereocontrol (Table 3.5.5). Modification of the phenyl group with electron-donating or mildly electron-withdrawing substituents in the ortho-, meta-, and para-positions is tolerated (Table 3.5.5, entries 1-7, 11). Diastereoselectivities are lower than with substrates represented in Table 3.5.4 but still in the practically useful range of greater than 10:1, and in most cases, the diastereomers are separable by column chromatography.

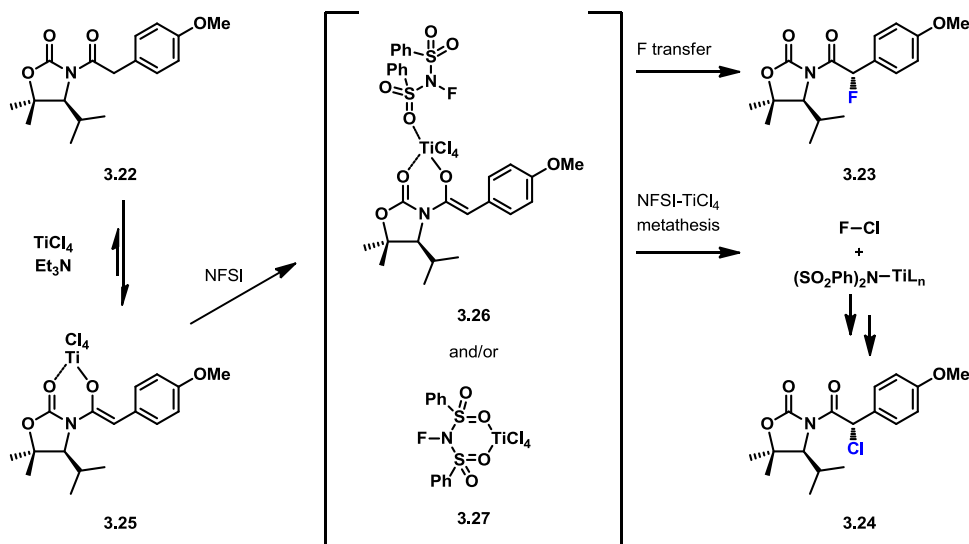
In addition, heteroaromatic substituents can effectively afford α -fluorination products with high diastereoselectivity, as demonstrated with the derivatives of 3-furanacetic acid (Table 3.5.5, entry 8) and 2-(benzo[*d*]oxazol-5-yl)acetic acid (Table 3.5.5, entry 10). On the other hand, fluorination of oxazolidinone derived from 2-(benzo[*d*]oxazol-2-yl)acetic acid (Table 3.5.5, entry 11) afforded a 2:1 mixture of diastereomers. The reduction in diastereoselectivity may be attributed to increased C–H acidity of this compound resulting in the enolization of products. Isolation of difluorination products observed for these examples supports this hypothesis.

Table 3.5.5 Scope of α -Fluorination of α -Aryl Acetic Acid *N*-Acyl Oxazolidinone Derivatives^{a,b,c}



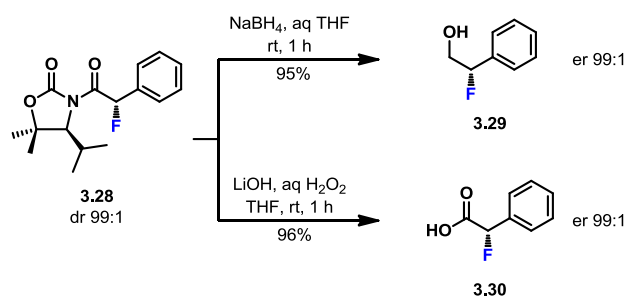
(a) Yields are of isolated pure major diastereomers unless indicated otherwise. Diastereomer ratios were determined by 600 MHz ^1H NMR analysis of the crude mixture of products. (b) Standard conditions: substrate (0.50 mmol), $\text{TiCl}_2(\text{OPr-}i)_2 \cdot 2\text{Et}_3\text{NHCl}$ (1.75 equiv), Et_3N (2.0 equiv), NFSI (2.0 equiv), CH_2Cl_2 (0.5 M), mixed and stirred at room temperature for 1 h. (c) Less than 10% of chlorinated products were observed along with products entries 2-11. (d) $\text{Ti}(\text{OPr-}i)_2\text{Cl}_2$ (1.75 equiv) was used; product isolated as a mixture of diastereomers.

Scheme 3.5.1 Mechanistic Hypothesis for the α -Fluorination Reaction



A plausible mechanism outlined in Scheme 3.4.1 accounts for the experimental observations, including higher than expected reactivity of titanium enolates in the electrophilic fluorination as well as the appearance of α -chlorination byproduct **3.24**. Soft enolization of 4-methoxyphenyl derivative **3.22** with TiCl_4 and Et_3N affords the expected Ti enolate. This newly formed Lewis acid could activate NFSI directly to form **3.26**, or NFSI could be activated by excess TiCl_4 to form **3.27**. The latter mode of activation may explain the need for 1.5–1.75 equiv of the reagent required for complete conversion. Activation of the NFSI by Lewis acid was documented to be essential for electrophilic fluorination of enolates by others.^{108e,117} Subsequent electrophilic fluorination typically affords **3.23** as the major product. Concurrently, a group exchange between Cl-TiL_n reagent (**3.26**, **3.27**, or other) and NFSI may take place giving rise to chlorine(I) fluoride, which is an electrophilic source of chloronium. When ClF reacts with the titanium enolate, α -chlorination product **3.24** is formed.¹¹⁸ The kinetics of these processes is likely affected by the identity of the Ti reagent among other reaction parameters.

Scheme 3.5.2 Preparation of Enantioenriched Fluorinated Building Blocks via Hydrolytic and Reductive Removal of the Chiral Auxiliary

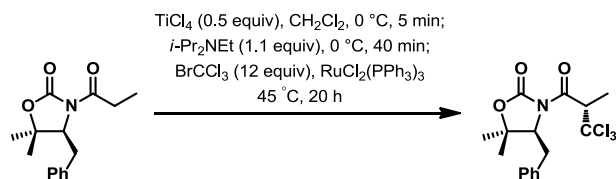


Conversion of the reaction products to broadly useful fluorinated building blocks for organic synthesis is illustrated by examples in Scheme 3.4.2. These include hydrolytic and reductive removal of the chiral auxiliary. The monofluorinated derivative **3.28** could be readily reduced using sodium borohydride in aqueous THF, delivering the corresponding fluoroalcohol **3.29** in high yields and with a high level of retention of stereochemical integrity. Compound **3.28** could also be hydrolyzed with a LiOH–H₂O₂ reagent system to yield the corresponding acid **3.30** in high yields and virtually complete preservation of stereochemistry. Notably, these transformations are characterized by excellent yields and nearly quantitative recovery of the chiral auxiliary.

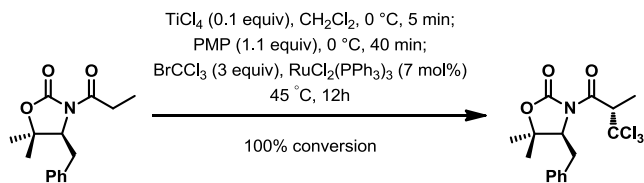
We have reported an operationally simple asymmetric α -fluorination reaction of *N*-acyl oxazolidinones based on the unique reactivity of group IVa metal enolates. From a practical perspective, the reaction requires inexpensive reagents, mild conditions, short reaction times at ambient temperatures, and delivers α -fluorination products directly in good yields and high diastereoselectivities.^{119,120} Ongoing studies are directed at defining a more detailed picture of the mechanism for the fluorination of α -arylacetic acid derivatives and determination of the structure and function of the $\text{TiCl}_2(\text{OPr-}i)_2 \cdot 2\text{Et}_3\text{NHCl}$ complex.

Chapter 3: Supporting Information

3-6: Dual Ti-Ru Catalysis Supporting Information



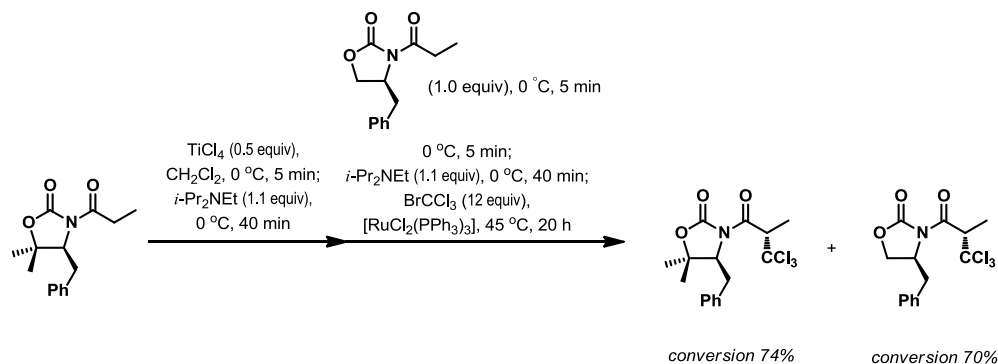
Titanium tetrachloride (1.0 M in CH_2Cl_2 , 0.25 ml, 0.25 mmol, 0.50 eq) was added to a solution of the substrate **3.1** (0.131 g, 0.50 mmol) in CH_2Cl_2 (0.75 ml) in a vial at 0 °C and the mixture was stirred for 5 min at the same temperature. Diisopropylethylamine (96 μl , 0.55 mmol, 1.1 eq) was added and the resulting deep red mixture was stirred at 0 °C for 40 min. Bromotrichloromethane (0.60 ml, 6.0 mmol, 12 eq) was added, followed by $\text{RuCl}_2(\text{PPh}_3)_3$ (34 mg, 0.035 mmol, 7 mol%) and the mixture was sealed and heated at 45 °C for 20 h. After cooling to room temperature, the reaction was quenched by adding water and extracted with CH_2Cl_2 . The organic layer was washed with brine and dried over Na_2SO_4 . After filtration and concentration, the crude product was analyzed by ^1H NMR spectroscopy indicating >97% conversion.



Titanium tetrachloride (1.0 M in CH_2Cl_2 , 0.10 ml, 0.10 mmol, 0.1 eq) was added to a solution of 4-benzyl-5,5-dimethyl-N-propionyloxazolidin-2-one (0.261 g, 1.0 mmol) in CH_2Cl_2 (1.2 ml) in a vial at 0 °C and the mixture was stirred for 5 min at the same temperature. 1,2,2,6,6-Pentamethylpiperidine (0.20 ml, 1.10 mmol, 1.1 eq) was added and

the resulting deep red mixture was stirred at 0 °C for 40 min. Bromotrichloromethane (0.30 ml, 3.0 mmol, 3 eq) was added, followed by $\text{RuCl}_2(\text{PPh}_3)_3$ (68 mg, 0.070 mmol, 7 mol%) and the mixture was sealed and heated at 45 °C for 12 h. After cooling down, the reaction was quenched by adding water and extracted with CH_2Cl_2 . The organic layer was washed with brine and dried over Na_2SO_4 . After filtration and concentration, the residue was analyzed by ^1H NMR spectroscopy, which indicated a 100% conversion. Purification by column chromatography on silica gel afforded the product (0.368 g, 0.97 mmol, 97%). ^1H NMR (400 MHz, CDCl_3); δ (ppm): 7.38-7.20 (m, 5H); 5.31 (q, $J=6.4$ Hz, 1H); 4.53(dd, $J_1=2.8$ Hz, $J_2=10.4$ Hz, 1H); 3.27 (dd, $J_1=2.8$ Hz, $J_2=14.4$ Hz, 1H); 2.81(dd, $J_1=10.4$ Hz, $J_2=14.4$ Hz, 1H); 1.60 ($J=6.4$ Hz, 3H); 1.34 (s, 3H); 1.30 (s, 3H).

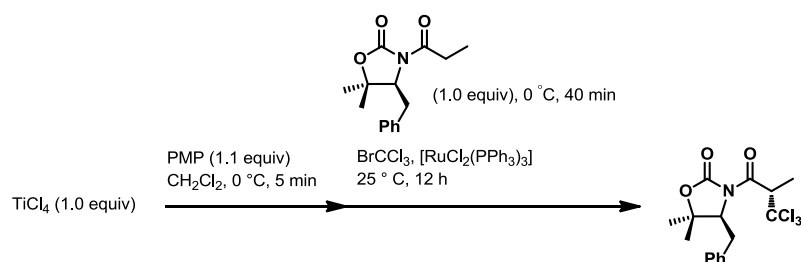
The crossover experiment:



Titanium tetrachloride (1.0 M in CH_2Cl_2 , 0.25 ml, 0.25 mmol) was added to a solution of the substrate **3.1** (0.131 g, 0.50 mmol, 1.0 eq) in CH_2Cl_2 (0.75 mL) in a vial at 0 °C and the mixture was stirred for 5 min at the same temperature. Diisopropylethylamine (96 μl , 0.55 mmol, 1.1 eq) was added and the resulting deep red mixture was stirred at 0 °C for 40 min. Oxazolidinone **3.6** (0.117 g, 0.50 mmol, 1.0 eq) in CH_2Cl_2 (0.4 ml) was added to the above reaction mixture and 5 min later $i\text{-Pr}_2\text{NEt}$ (96 μl , 0.55 mmol, 1.1 eq) was added. After

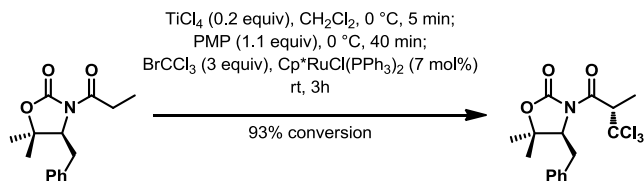
stirring for additional 40 min at 0 °C, BrCCl₃ (0.60 ml, 6.0 mmol, 12 eq) and RuCl₂(PPh₃)₃ (34 mg, 0.035 mmol, 7 mol%) were added, and the mixture was sealed and heated at 45 °C for 20 h. After cooling down, the reaction was quenched by adding water and extracted with CH₂Cl₂. The organic layer was washed with brine and dried over Na₂SO₄. After filtration and concentration, the residue was analyzed by ¹H NMR, which indicated a clean transformation with a 74% conversion of **3.1** and 70% conversion of **3.6**.

The effects of the order of addition of reagents:



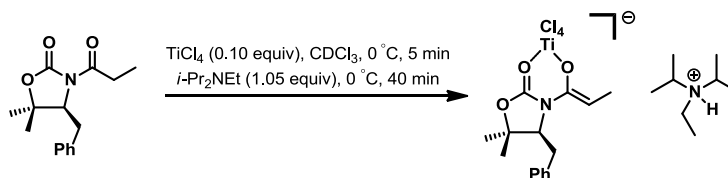
1,2,2,6,6-Pentamethylpiperidine (0.10 ml, 0.55 mmol) was added to a solution of TiCl₄ (1.0 M in CH₂Cl₂, 0.50 ml, 0.50 mmol, 1.0 eq) at 0 °C and stirred for 5 min. A solution of **3.1** (0.131 g, 0.50 mmol, 1.0 eq) in CH₂Cl₂ (1.2 ml) was added. After stirring at the same temperature for 40 min, BrCCl₃ (0.15 ml, 1.50 mmol, 3 eq) and RuCl₂(PPh₃)₃ (34 mg, 0.035 mmol, 7 mol%) were added, and the mixture was allowed to stir at room temperature for 12 h. After cooling down, the reaction was quenched by adding water and extracted with CH₂Cl₂. The organic layer was washed with brine and dried over Na₂SO₄. After filtration and concentration, the residue was monitored by ¹H NMR with a conversion of 57%.

The effect of Ru-catalyst:



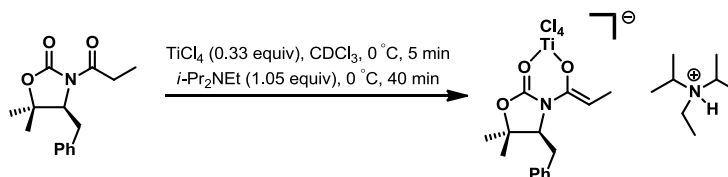
Titanium tetrachloride (1.0 M in CH_2Cl_2 , 0.10 ml, 0.10 mmol, 0.2 eq) was added to a solution of the substrate **3.1** (0.131 g, 0.50 mmol, 1.0 eq) in CH_2Cl_2 (1.2 ml) in a vial at $0\text{ }^\circ\text{C}$ and the mixture was stirred for 5 min at the same temperature. PMP (0.10 ml, 0.55 mmol, 1.1 eq) was added and the resulting deep red mixture was stirred at $0\text{ }^\circ\text{C}$ for 40 min. Bromotrichloromethane (0.15 ml, 1.5 mmol, 3 eq) was added, followed by $\text{Cp}^*\text{RuCl}(\text{PPh}_3)_2$ (28 mg, 0.035 mmol, 7 mol%) and the mixture was stirred at room temperature. The reaction was monitored by TLC indicating around 90% conversion after 1.5 h, and the reaction was quenched at 3 h by adding water. The mixture extracted with CH_2Cl_2 and the organic layer was washed with brine and dried over Na_2SO_4 . The conversion was 93% measured by ^1H NMR of the crude material.

^1H NMR Studies of enolization in CDCl_3 :

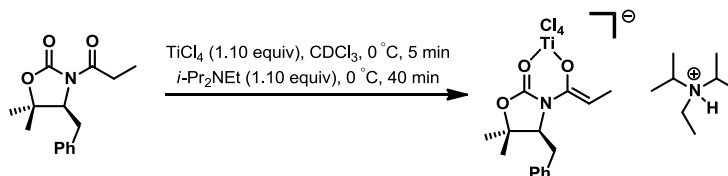


Titanium tetrachloride (1.0 M in CDCl_3 , 0.15 ml, 0.15 mmol, 0.1 eq) was added to a solution of the substrate **3.1** (0.392 g, 1.50 mmol, 1.0 eq) in CDCl_3 (5.2 ml) in a vial at $0\text{ }^\circ\text{C}$ and the mixture was stirred for 5 min at the same temperature. Diisopropylethylamine (0.274 ml, 1.58 mmol, 1.05 eq) was added and the resulting deep red mixture was stirred at $0\text{ }^\circ\text{C}$ for 40

min. The reaction mixture was transferred via cannula to a NMR tube which was pre-filled with Ar.



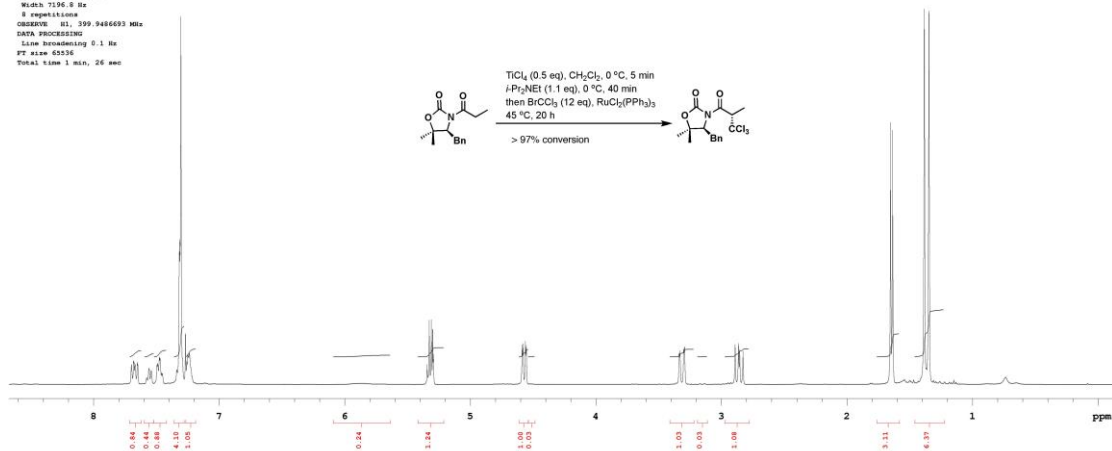
Titanium tetrachloride (1.0 M in CDCl_3 , 0.17 ml, 0.17 mmol, 0.33 eq) was added to a solution of the substrate **3.1** (0.136 g, 0.52 mmol, 1.0 eq) in CDCl_3 (1.8 ml) in a vial at 0°C and the mixture was stirred for 5 min at the same temperature. Diisopropylethylamine (95 μl , 0.55 mmol, 1.05 eq) was added and the resulting deep red mixture was stirred at 0°C for 40 min. The reaction mixture was transferred via cannula to a NMR tube which was pre-filled with Ar.



Titanium tetrachloride (1.0 M in CDCl_3 , 0.58 ml, 0.58 mmol, 1.1 eq) was added to a solution of the substrate **3.1** (0.138 g, 0.53 mmol, 1.0 eq) in CDCl_3 (1.8 ml) in a vial at 0°C and the mixture was stirred for 5 min at the same temperature. Diisopropylethylamine (0.10 ml, 0.58 mmol, 1.1 eq) was added and the resulting deep red mixture was stirred at 0°C for 40 min. The reaction mixture was transferred via cannula to a NMR tube which was pre-filled with Ar.

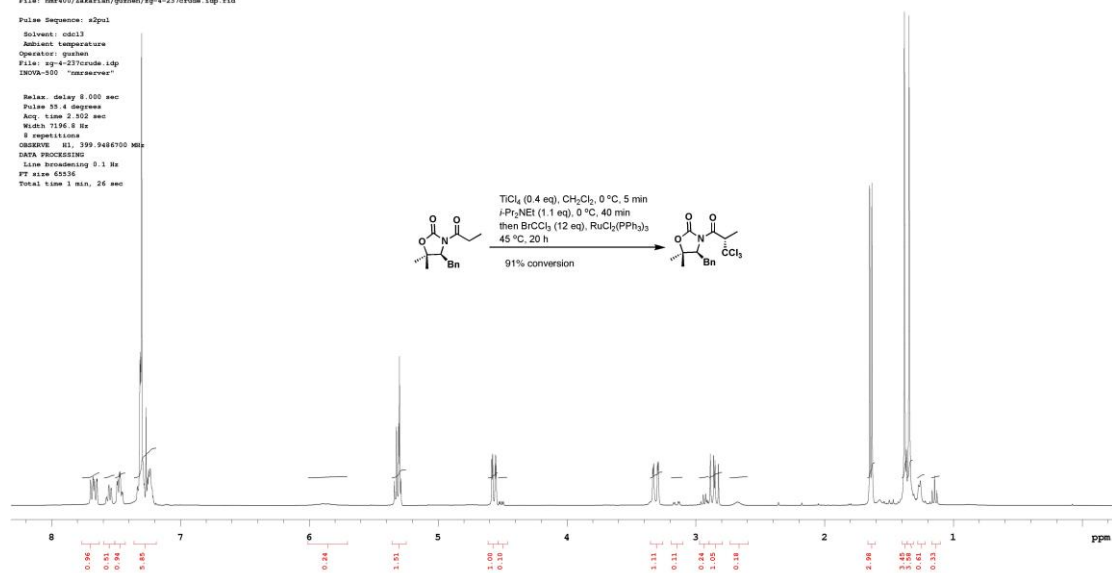
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 Ambient temperature
 Operator: guhen
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 INOVA-500 "nmrserver"

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 8 repetitions
 CDSFREQ: 51.399 946603 MHz
 DATA PROCESSING
 Line broadening 0.1 Hz
 FT size 65536
 Total time 1 min, 26 sec



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Solvent: cdcl3

Acquisition temperature

Operator: gushen

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8 repetitions

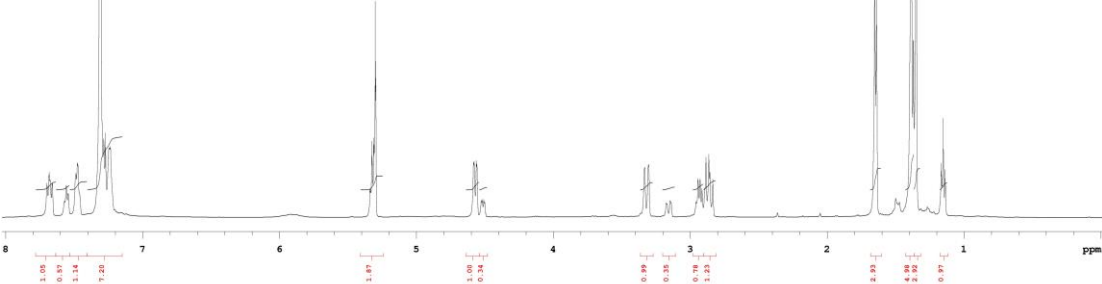
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DATA PROCESSING

Line broadening 0.2 Hz

FT size 32768

Total time 1 min, 24 sec



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Solvent: cdcl3

Acquisition temperature

Operator: gushen

File: sp-4-240crude.idp

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Aq. time 2.500 sec

Width 7196.8 Hz

8 repetitions

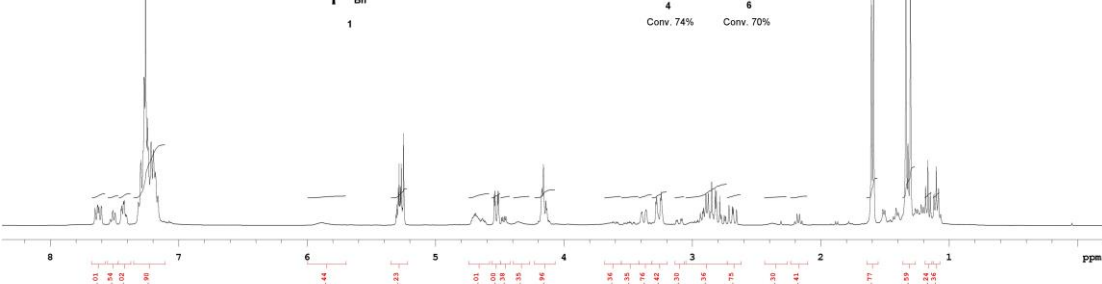
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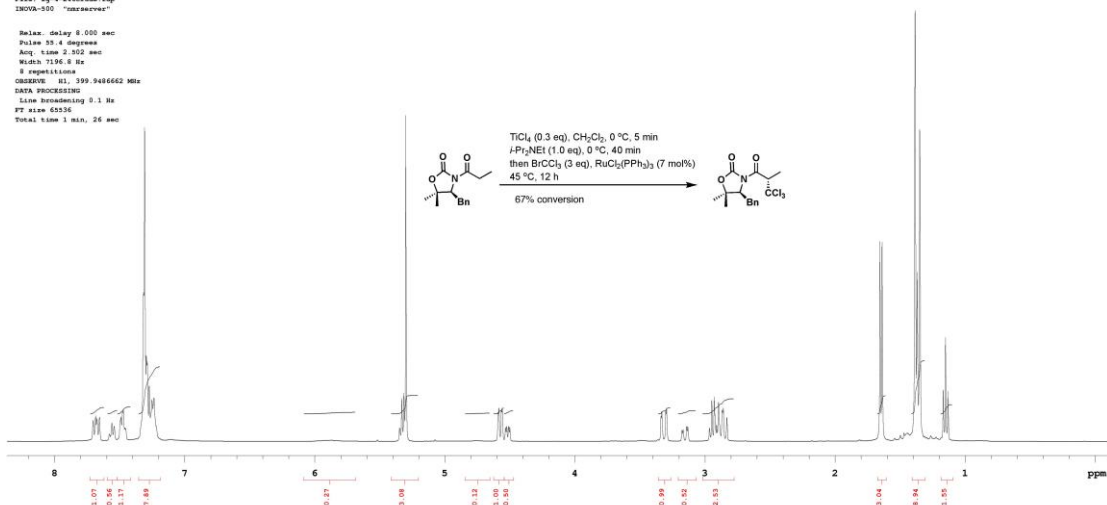
Line broadening 0.1 Hz

FT size 65536

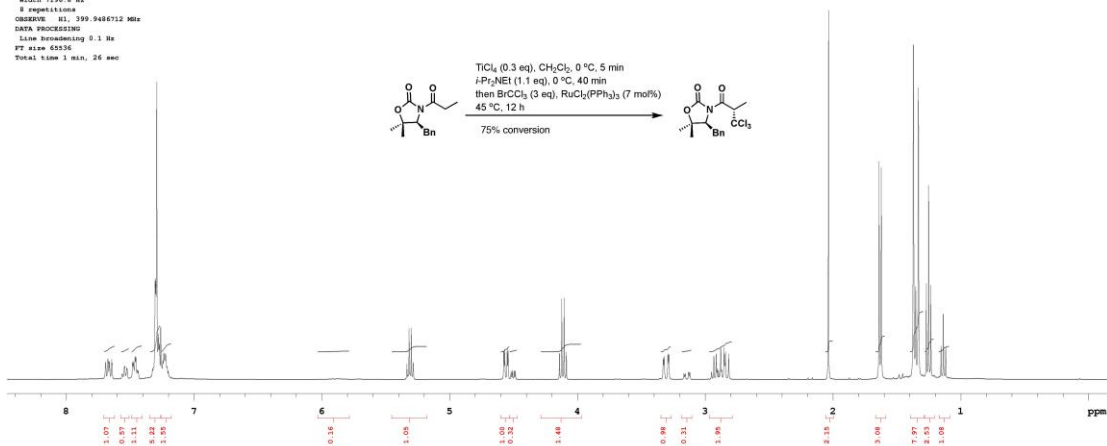
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 Substant: Temperature
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 Pulse 30.4 degrees
 Acq. time 2.302 sec
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 8 repetitions
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 DATA PROCESSING
 Line Broadening 0.1 Hz
 FT size 65536
 Total time 1 min, 26 sec



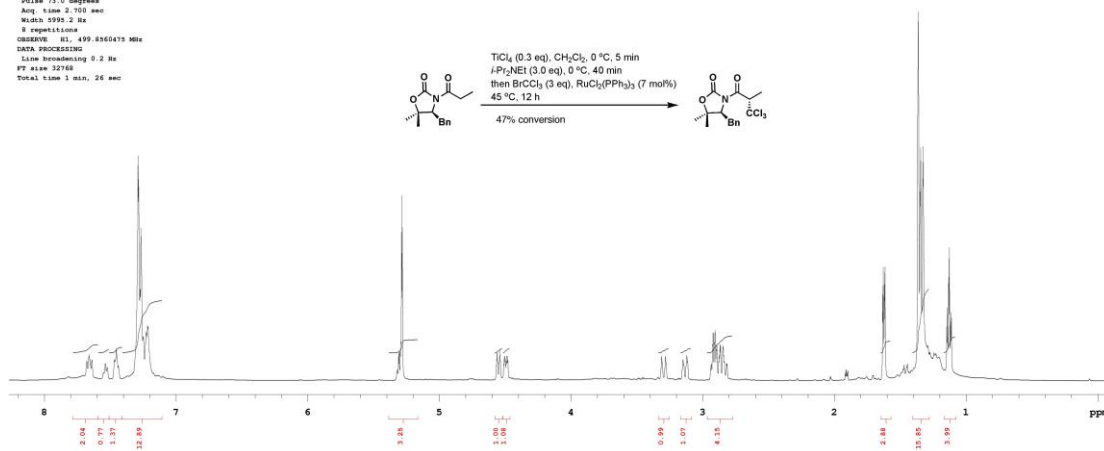
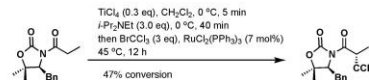
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 Total time 1 min, 26 sec



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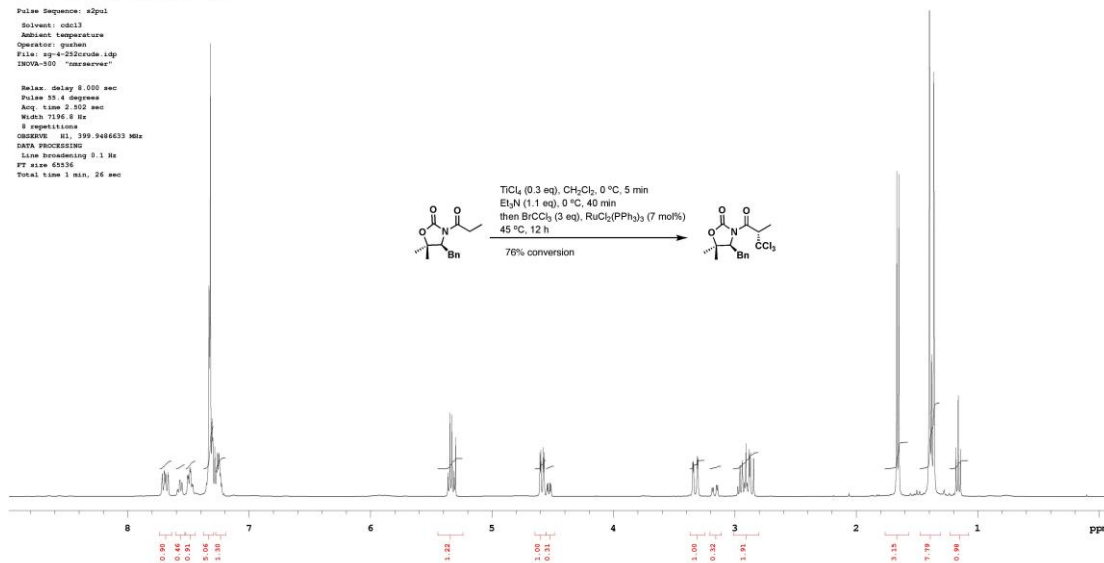
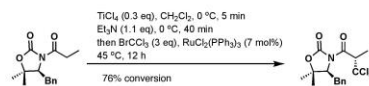
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DATA PROCESSING
Line broadening 0.2 Hz
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Total time 1 min, 24 sec



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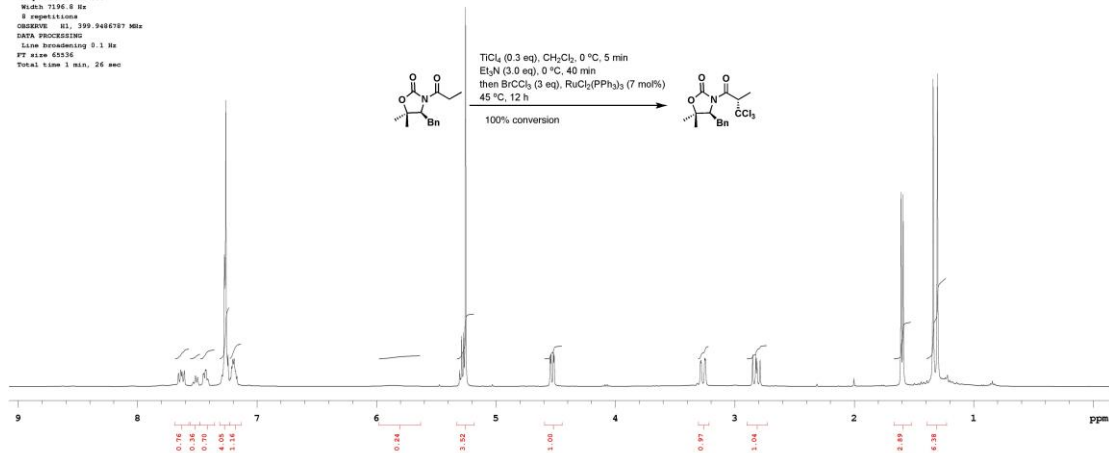
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Operator: gushen
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Acq. time 2.502 sec
Width 7196.8 Hz
S repetitions
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DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 24 sec



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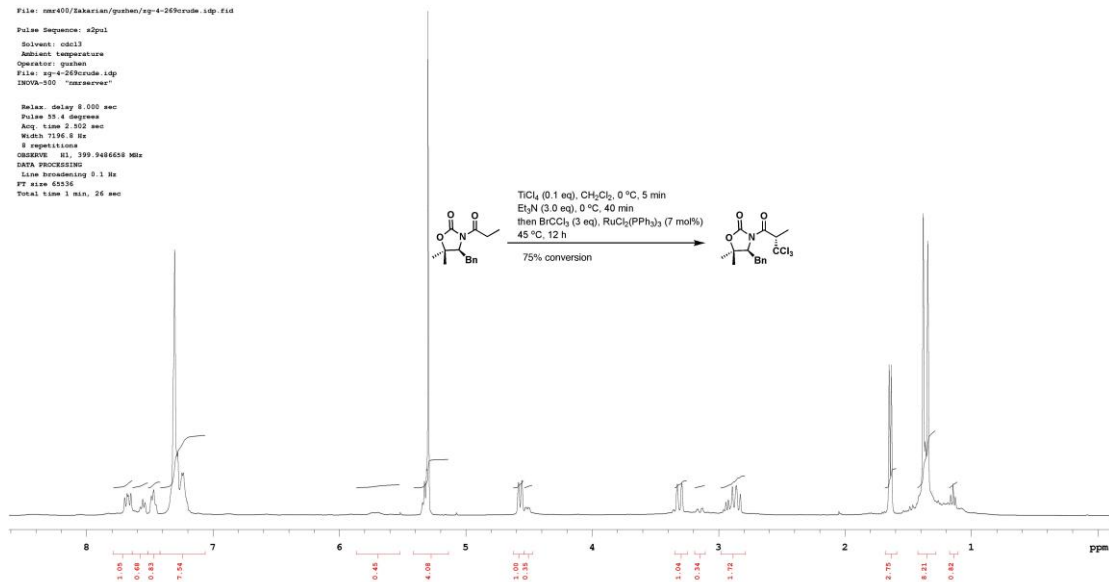
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Operator: guhen
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INSTRUMENT: spect
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Pulse: 30.4 degrees
Acq. time: 2.302 sec
Width: 7196.8 Hz
8 repetitions
OBSERVE: H1, 399.9486787 MHz
DATA PROCESSING
Line Broadening: 0.1 Hz
FT size: 65536
Total time: 1 min, 26 sec



sp-4-263crude.idp

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Solvent: cdcl3
Subsant Temperature
Operator: guhen
File: sp-4-263crude.idp
INSTRUMENT: spect
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Pulse: 30.4 degrees
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8 repetitions
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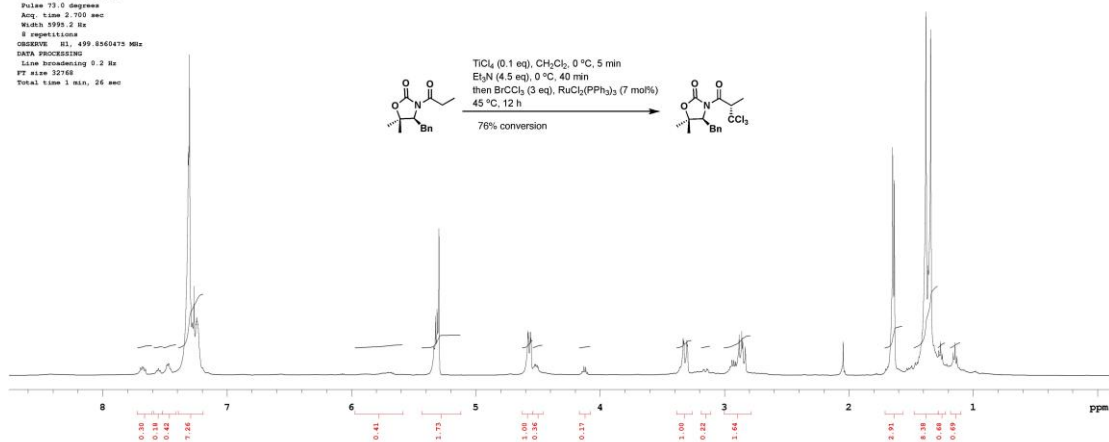


sp-4-270crude.500
short silica pad

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INVOA-500 "nmrserver"

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DATA PROCESSING
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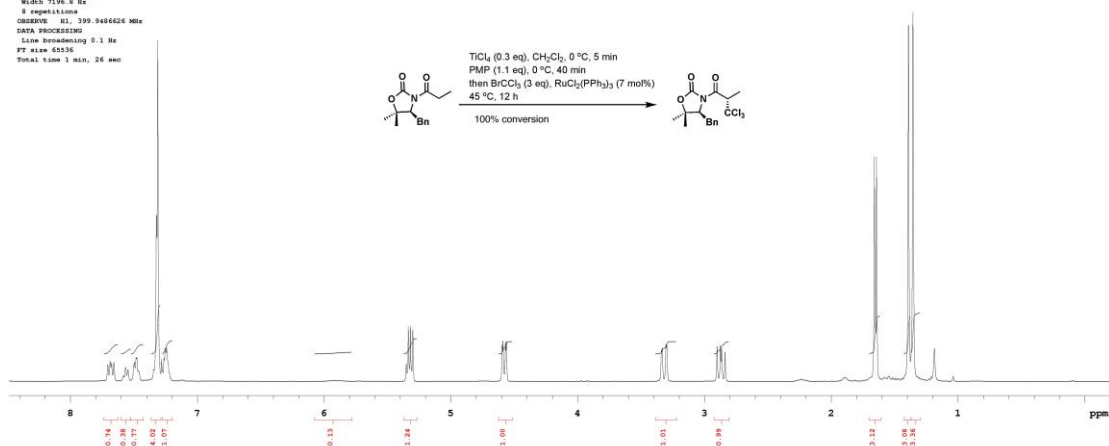


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Subsant temperature
Operator: gushen
File: sp-4-284crude.idp
INVOA-500 "nmrserver"

Relax. delay 8.000 sec
Pulse 55.4 degrees
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Width 7196.8 Hz
8 repetitions
OBSERVE H1 399.948626 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 3 min, 24 sec

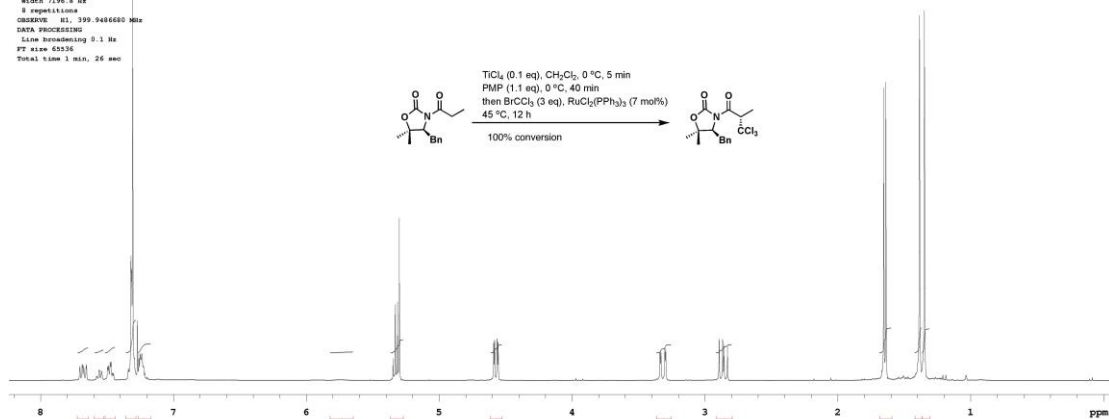


sp-4-266crude.idp

File: nmr405/Zakaria/guhen/sp-4-266crude.idp.Fid

Pulse Sequence: zgpg30
Solvent: cdcl3
Subsant Temperature
Operator: guhen
File: sp-4-266crude.idp
1300A-500 "unrecrver"

Pulse Delay 8.000 sec
Pulse 51.4 degrees
Acq. time 2.302 sec
Nuclei 13C
8 repetitions
GHSNVE H1 399.9486680 MHz
DATA PROCESSING
Low Broadening 0.1 Hz
FT size 65536
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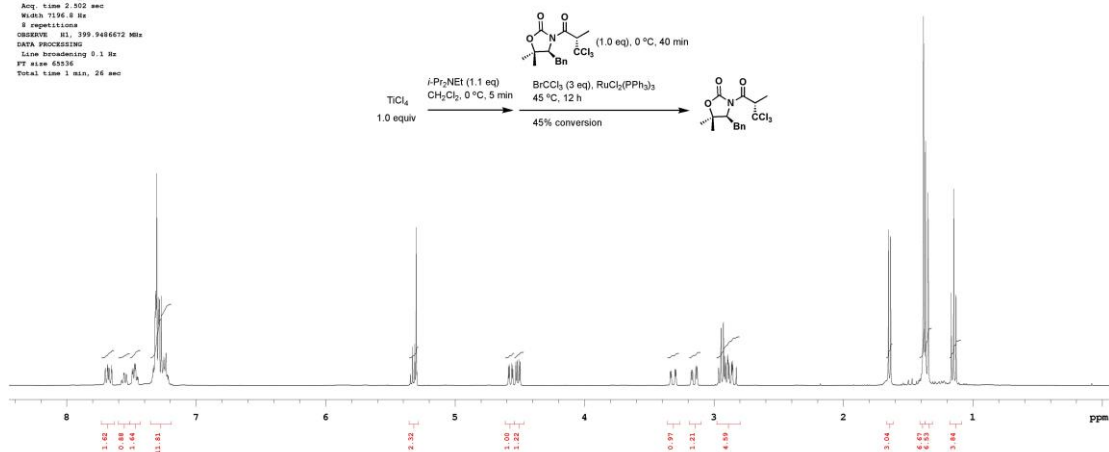


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Subsant Temperature
Operator: guhen
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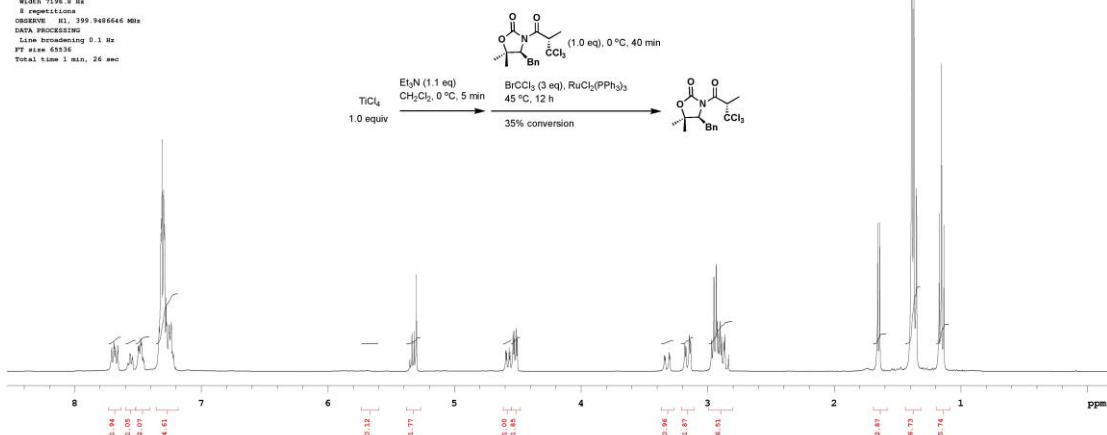
Pulse Delay 8.000 sec
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Acq. time 2.302 sec
Nuclei 13C
8 repetitions
GHSNVE H1 399.9486672 MHz
DATA PROCESSING
Low Broadening 0.1 Hz
FT size 65536
Total time 1 min, 24 sec



sp-4-278crude.idp

File: nmr405/Ekharan/guhen/sp-4-278crude.idp.Fid

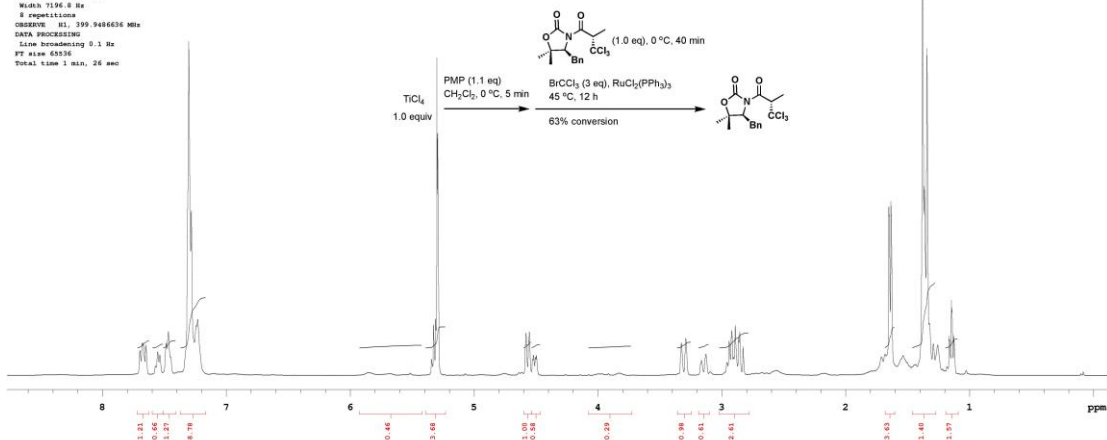
Pulse Sequence: zgpg30
Solvent: cdcl3
Ambient temperature
Operator: guhen
File: sp-4-278crude.idp
INVOA-500 "nucserver"
Relax: delay 8.000 sec
Pulse 55.4 degrees
Acq. time 2.502 sec
Width 7196.8 Hz
S repetitions
OBSERVE: H1, 399.9486646 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 24 sec



sp-4-278crude.idp

File: nmr405/Ekharan/guhen/sp-4-278crude.idp.Fid

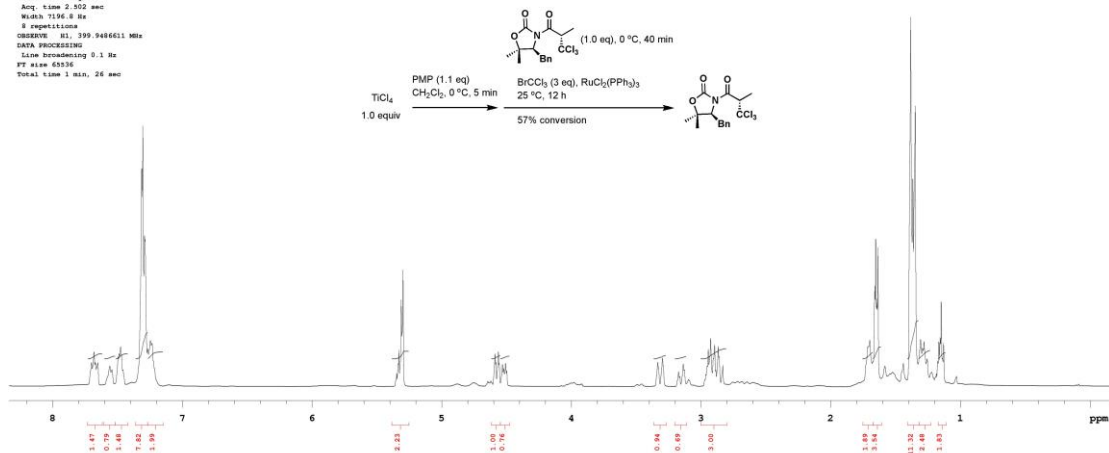
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Ambient temperature
Operator: guhen
File: sp-4-278crude.idp
INVOA-500 "nucserver"
Relax: delay 8.000 sec
Pulse 55.4 degrees
Acq. time 2.502 sec
Width 7196.8 Hz
S repetitions
OBSERVE: H1, 399.9486646 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 24 sec



sp-4-283crude.idp

File: nmr400/Ekharan/guhen/sp-4-283crude.idp.Fid

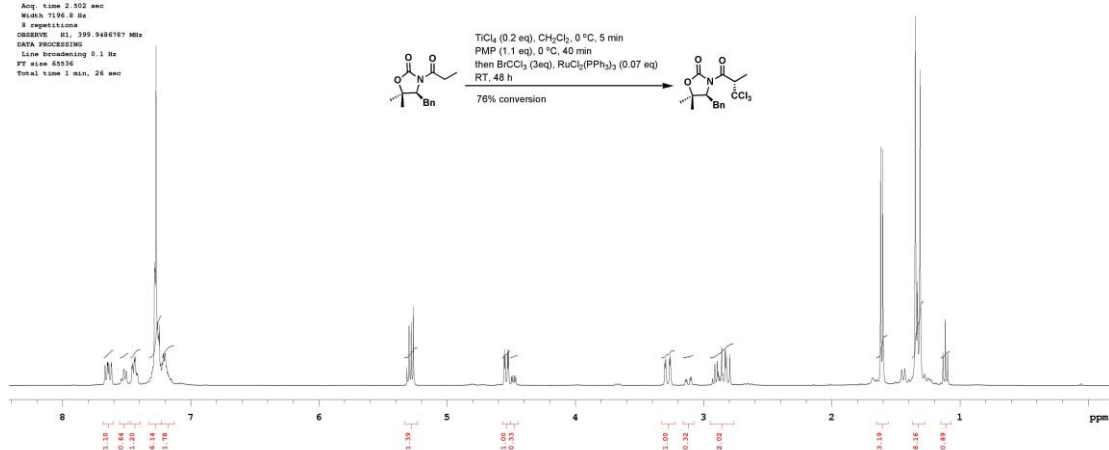
Pulse Sequence: zgpg30
Solvent: cdcl3
Ambient temperature
Operator: guhen
File: sp-4-283crude.idp
INSTRUMENT: spect
Relax: delay 8.000 sec
Pulse 55.4 degrees
Acq. time 2.502 sec
Width 7196.8 Hz
S repetitions
Sweep: HI: 399.9486611 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 24 sec



sp-4-277crude.idp

File: nmr400/Ekharan/guhen/sp-4-277crude.idp.Fid

Pulse Sequence: zgpg30
Solvent: cdcl3
Ambient temperature
Operator: guhen
File: sp-4-277crude.idp
INSTRUMENT: spect
Relax: delay 8.000 sec
Pulse 55.4 degrees
Acq. time 2.502 sec
Width 7196.8 Hz
S repetitions
Sweep: HI: 399.9486787 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 65536
Total time 1 min, 24 sec



sp-4-273crude.idp

File: nmr405/Sakarian/gushen/sp-4-273crude.idp.fid

Pulse Sequence: zgpg30

Solvent: cdcl3

Ambient temperature

Operator: gushen

File: sp-4-273crude.idp

INOVA-500 "nmrserver"

Relax. delay: 8.000 sec

Pulse: 50.4 degrees

Aq. time: 2.500 sec

Width: 7196.8 Hz

8 repetitions

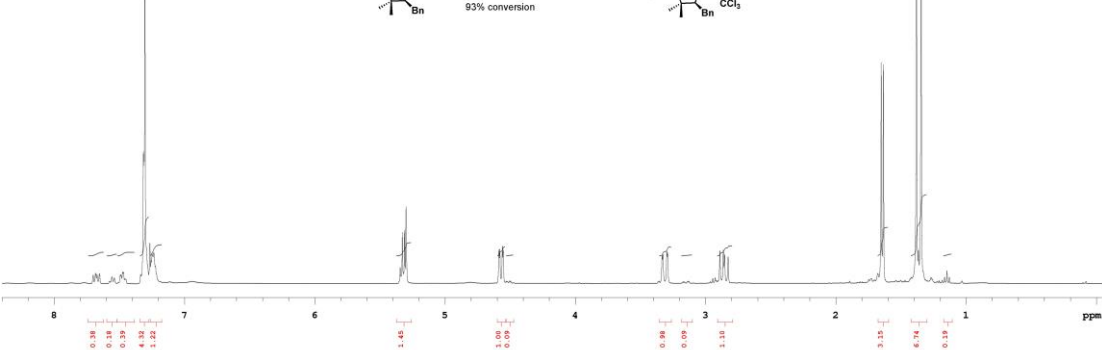
Observed: 500.13999486690 MHz

DATA PROCESSING

Line broadening: 0.1 Hz

FT size: 65336

Total time: 1 min, 24 sec



ath-2-064-c

3:1 (v/v) (TIC14)

500MHz

800 Probe

Sample: ath-2-064-c

File: nmr500/Sakarian/herma/ath-2-064-c.fid

Pulse Sequence: zgpg30

Solvent: CDCl₃

Ambient temperature

Operator: herma

File: ath-2-064-c

INOVA-500 "nmrserver"

Relax. delay: 8.000 sec

Pulse: 40.8 degrees

Aq. time: 2.500 sec

Width: 5995.2 Hz

16 repetitions

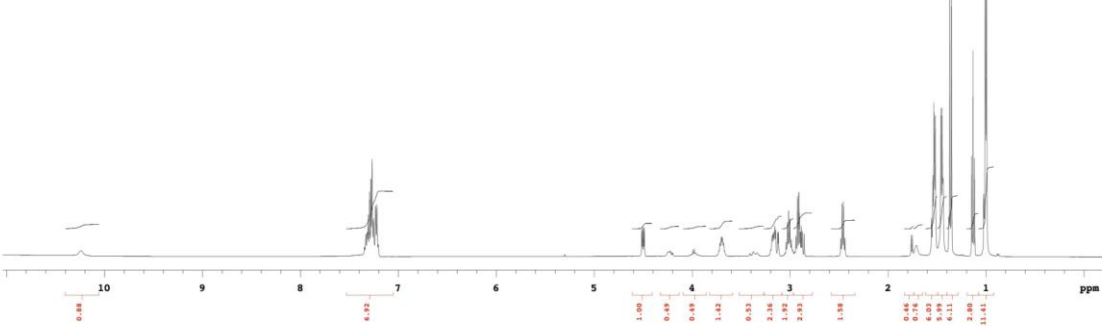
Observed: 500.13999486690 MHz

DATA PROCESSING

Line broadening: 0.2 Hz

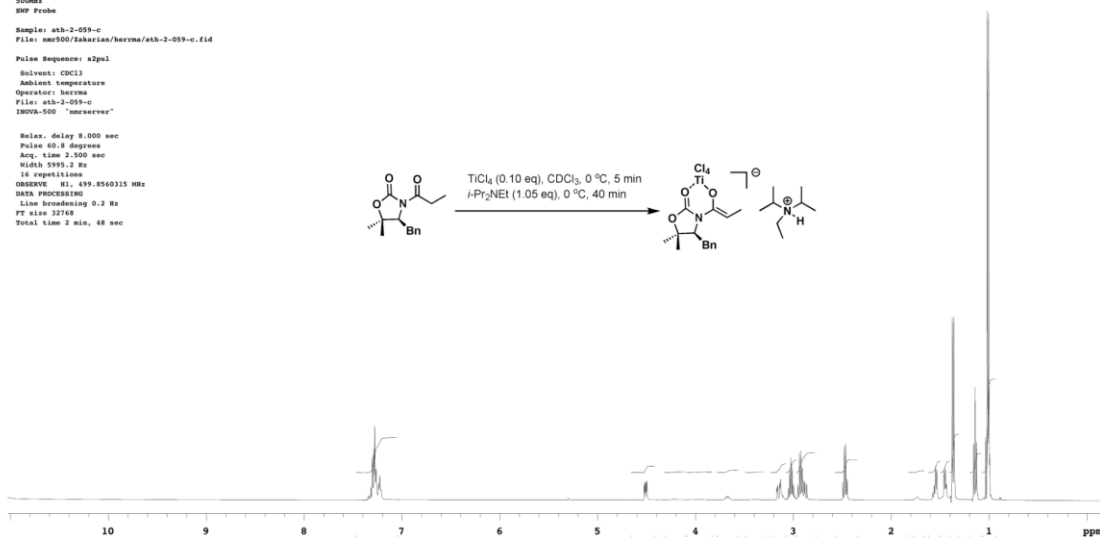
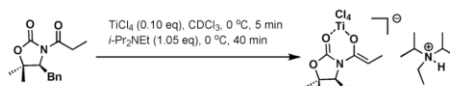
FT size: 32748

Total time: 2 min, 48 sec



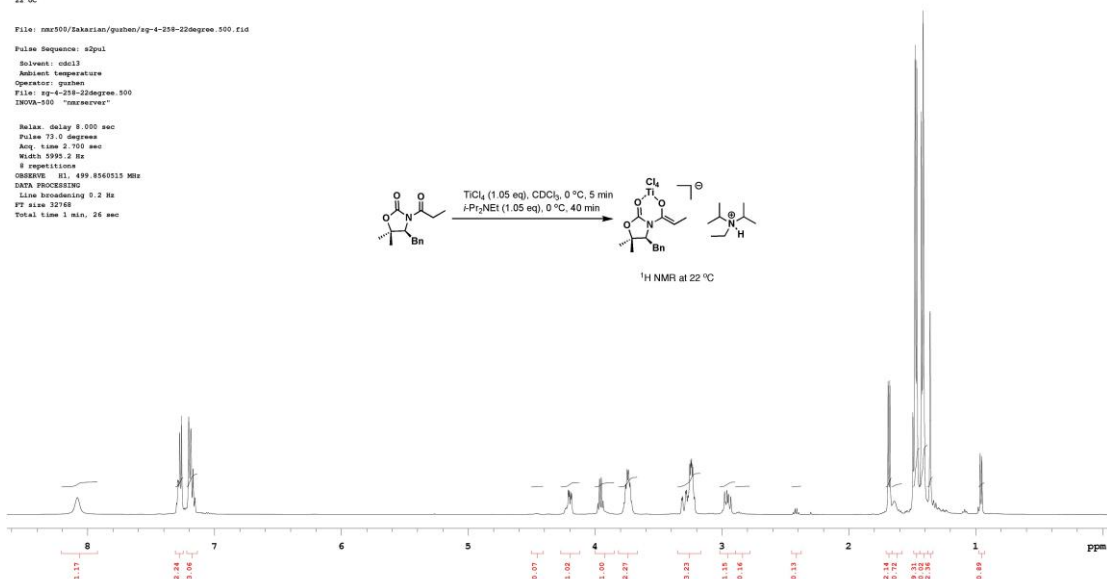
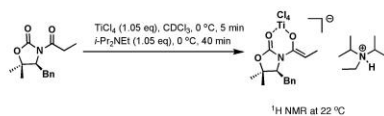
ath-2-059-c
 9:1 (cdh:TiCl4)
 500MHz
 SPP Probe
 Sample: ath-2-059-c
 File: nmr500/Sakarian/herma/ath-2-059-c.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 Operator: herma
 File: ath-2-059-c
 INOVA-500 "nucserve"

Relax. delay 8.000 sec
 Pulse 60.0 degrees
 Acq. time 2.500 sec
 Width 5595.2 Hz
 16 repetitions
 OBSERVE H1, 499.8560315 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 2 min, 48 sec



sp-4-258-500
 22 °C
 File: nmr500/Sakarian/guhen/sp-4-258-22degree.500.r16
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Ambient temperature
 Operator: guhen
 File: sp-4-258-22degree.500
 INOVA-500 "nucserve"

Relax. delay 8.000 sec
 Pulse 73.0 degrees
 Acq. time 2.705 sec
 Width 5595.2 Hz
 8 repetitions
 OBSERVE H1, 499.8560315 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 24 sec



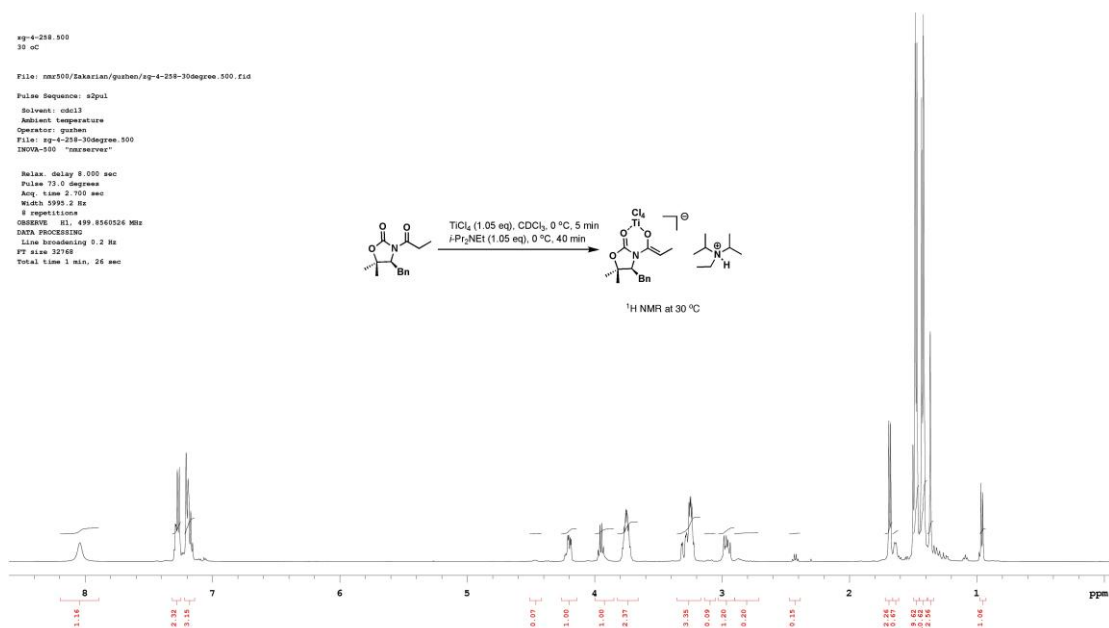
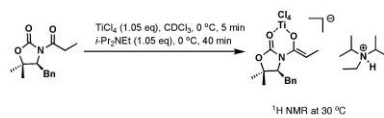
sp-4-258.500
30 uC

File: nmz500/zakarian/gushen/sp-4-258-30degree.500.f16

Pulse Sequence: zgpg30

Solvent: cdcl3
Subvent temperature
Operator: gushen
File: sp-4-258-30degree.500
INVOG-500 "nmzserver"

Relax. delay 9.000 sec
Pulse 73.0 degree
Acq. time 2.700 sec
Width 5595.2 Hz
repetitions
OBSERVE K1: 499.8560526 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 3 min. 26 sec



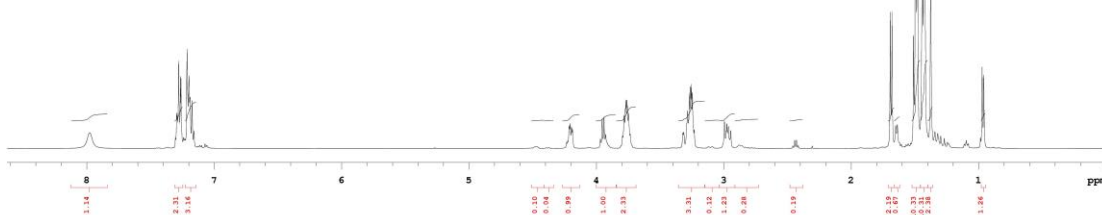
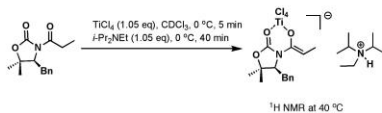
sp-4-258.500
40 °C

File: nmr500/Eskarian/gushen/sp-4-258-40degren.500.r16

Pulse Sequence: zgpg30

Solvent: cdcl3
Acquire temperature
Operator: gushen
File: sp-4-258-40degren.500
INSTRUMENT: "nmrserver"

Relax. delay 9.000 sec
Pulse 73.0 degrees
Acq. time 2.700 sec
Width 5090.2 Hz
F 9.999 MHz
S 1024
DATA PROCESSING
OBSERVE H1, 499.8560518 MHz
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 24 sec



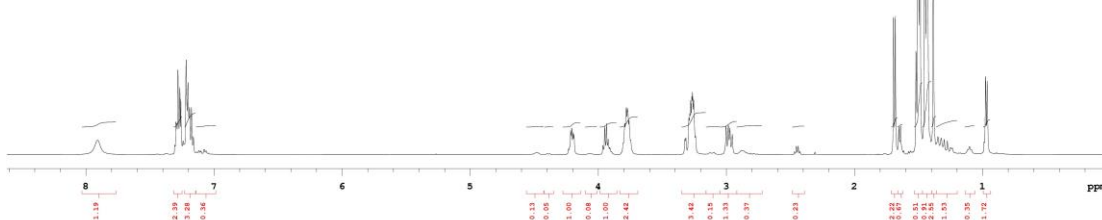
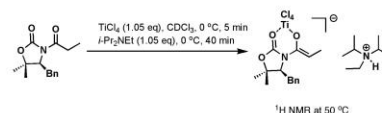
sp-4-258.500
50 °C

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Pulse Sequence: zgpg30

Solvent: cdcl3
Acquire temperature
Operator: gushen
File: sp-4-258-50degren.500
INSTRUMENT: "nmrserver"

Relax. delay 9.000 sec
Pulse 73.0 degrees
Acq. time 2.700 sec
Width 5090.2 Hz
F 9.999 MHz
S 1024
DATA PROCESSING
OBSERVE H1, 499.8560520 MHz
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 24 sec

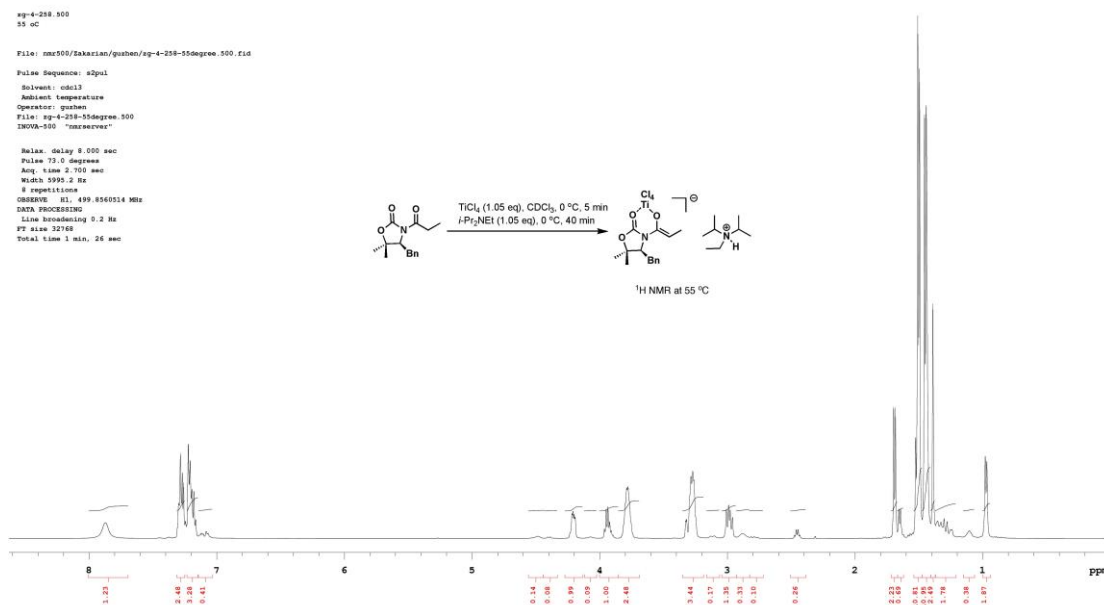
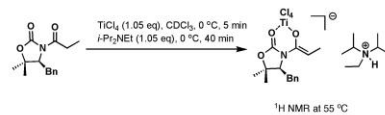


sp-4-258.500
55 uC

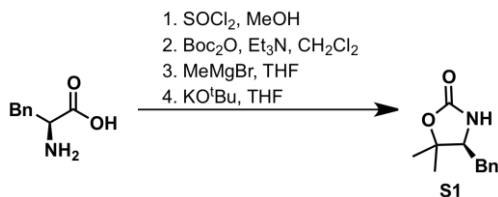
File: nmr500/zakarian/gushen/sp-4-258-55degree.500.f16

Pulse Sequence: zgpg30
Solvent: cdcl3
Subvent temperature
Operator: gushen
File: sp-4-258-55degree.500
INSTRUMENT: "nmrserver"

Relax. delay 9.000 sec
Pulse 73.0 degrees
Acq. time 2.700 sec
Width 5595.2 Hz
repetitions
OBSERVE K1: 499.8560514 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 3 min. 26 sec



3-7: Perfluoroalkylations of *N*-Acyl Oxazolidinones Supporting Information

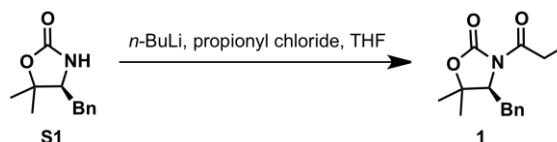


(*S*)-4-Benzyl-5,5-dimethyloxazolidin-2-one. Thionyl chloride (5.50 mL, 74.8 mmol) was added dropwise to a solution of *L*-phenylalanine (6.17 g, 37.4 mmol) in methanol (104 mL) at 0 °C. The reaction was stirred for 30 min at 0 °C, and then heated to reflux for 4 h. The solution was cooled to rt and methanol was removed *in vacuo*. The crude residue was submitted to the next step without purification.

Di-*tert*-butyl dicarbonate (8.08 g, 37.0 mmol) was added to a mixture of the crude substrate (37.4 mmol), triethylamine (5.70 mL, 41.4 mmol), and dichloromethane (83.0 mL) at rt. The reaction was stirred at rt for 2 h and then quenched with HCl (1M). The layers were separated. The aqueous layer was extracted with dichloromethane (3x30 mL). The combined organic layers were dried with sodium sulfate and concentrated *in vacuo* to afford a white solid. The crude residue was submitted to the next step without further purification.

Methylmagnesium bromide (3 M in Et₂O, 49.9 mL, 150 mmol) was added dropwise to a solution of the crude substrate (37.4 mmol) in THF (125 mL) at 0 °C. The reaction was stirred at 0 °C for 10 min, then warmed to rt and stirred for 36 h. The solution was cooled to 0 °C and quenched with methanol. The solvent was removed *in vacuo*, and the solids were re-dissolved in ethyl acetate and water. The layers were separated. The aqueous layer was extracted with ethyl acetate (3x75 mL). The combined organic layers were dried with sodium sulfate and concentrated *in vacuo* delivering a light yellow oil. The crude residue was submitted to the next step without further purification.

Potassium *tert*-butoxide (4.74 g, 42.2 mmol) was added to a solution of the crude substrate (37.4 mmol) in THF (101 mL) at 0 °C. The reaction was warmed to rt and stirred for 2.5 h. The reaction was then quenched with saturated aqueous ammonium chloride. The layers were separated. The aqueous layer was extracted with ethyl acetate (3x40 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The crude product was purified by column chromatography (silica, 40% ethyl acetate – hexanes, 60% ethyl acetate - hexanes) to afford the white/yellow solid oxazolidinone **S1** (6.31 g, 30.7 mmol, 82% over 4 steps)¹²¹. ¹H NMR (400 MHz, CDCl₃); δ(ppm): 7.37-7.32 (m, 1H); 7.30-7.23 (m, 1H); 7.19-7.16 (m, 2H); 4.69 (brs, 1H); 3.68 (dd, J1=10.8 Hz, J2=3.6 Hz, 1H); 2.84 (dd, J1=13.6 Hz, 3.6 Hz, 1H); 2.67 (dd, J1=13.6 Hz, J2=10.8 Hz, 1H); 1.50 (s, 3H); 1.47 (s, 3H).

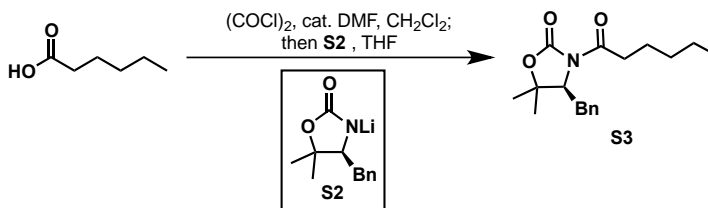


(S)-4-Benzyl-5,5-dimethyl-3-propionyloxazolidin-2-one (3.12). *n*-Butyllithium (10.4 mL, mmol, 2.45 M in hexanes) was added to a solution of the oxazolidinones **S1** (5.00 g, 24.4 mmol) in THF (81.3 mL) at -78 °C. After 30 min, propionyl chloride (2.16 mL, 24.9 mmol) was added and the reaction was stirred for an additional 30 min. The reaction was warmed to 0 °C and stirred for 1.5 h. The reaction was quenched with saturated aqueous ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3x100 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated, and purified by column chromatography (silica, 30% ethyl acetate - hexanes) to afford the desired product (5.93 g, 24.5 mmol, 93%). α_D^{22} -29.3° (c 1.0,

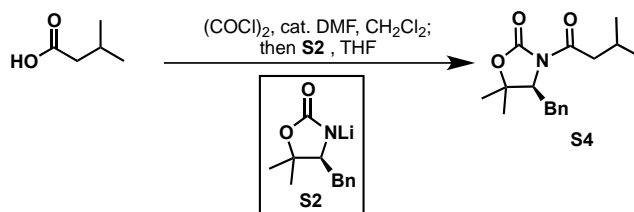
dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.32-7.25 (m, 4H); 7.25-7.20 (m, 1H); 4.50 (dd, $J_1=10.2$ Hz, $J_2=4.2$ Hz, 1H); 3.15 (dd, $J_1=15.0$ Hz, $J_2=4.2$ Hz, 1H); 2.98-2.88 (m, 2H); 2.88 (dd, $J_1=4.2$ Hz, $J_2=15.0$ Hz, 1H); 1.37 (s, 3H); 1.36 (s, 3H); 1.14 (dd, $J_1=J_2=7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 174.5, 152.9, 137.2, 129.3 (2C), 128.9 (2C), 127.0, 82.4, 63.7, 35.6, 29.6, 28.8, 22.5, 8.6. LRMS (ESI) calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_3\text{Na}$ [M+Na] 284.1263, found 284.14.

Standard procedure for the synthesis of *N*-acyl oxazolidinones:

Oxalyl chloride (0.96 mL, 11.0 mmol) was added to a solution of carboxylic acid (1.26 mL, 10.0 mmol), dimethylformamide (10 μL), and dichloromethane (3.30 mL) at 0 °C. After 10 min, the solution was warmed to rt and stirred for 1 h (until bubbling stops). The solution was concentrated on a rotary evaporator. In a separate flask, *n*-butyllithium (2.48 M in hexanes, 2.82 mL, 7.0 mmol), was added to a solution of oxazolidinone **S1** (1.37 g, 6.67 mmol) in THF (18.2 mL) at -78 °C under argon. The solution was stirred for 30 min at -78 °C. A solution of the crude acyl chloride in THF (16.7 mL total with rinses) was added dropwise at -78 °C. After stirring at -78 °C for 2 h, the reaction mixture was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated on a rotary evaporator. The resultant oil or solid was purified by column chromatography to give the corresponding *N*-acyl oxazolidinone.

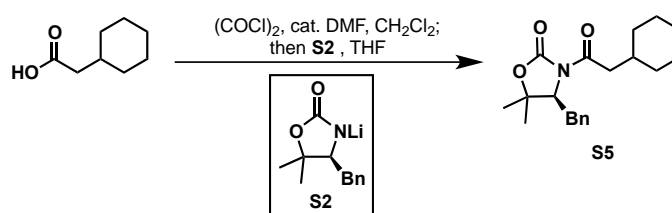


(S)-4-Benzyl-3-hexanoyl-5,5-dimethyloxazolidin-2-one (3.31). The title compound was prepared from commercially available hexanoic acid (0.630 mL, 5.00 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a colorless oil (1.17 g, 3.86 mmol, 77%) after purification by column chromatography (silica, 30% ethyl acetate - hexanes). α_D^{23} -28.8° (c 1.0, dichloromethane). ^1H NMR (400 MHz, CDCl_3); δ (ppm): 7.34-7.20 (m, 5H); 4.51 (dd, $J_1=9.6$ Hz, $J_2=4.0$ Hz, 1H); 3.13 (dd, $J_1=14.4$ Hz, $J_2=4.0$ Hz, 1H); 2.98-2.82 (m, 3H); 1.68-1.60 (m, 2H); 1.37 (s, 3H); 1.35 (s, 3H); 1.40-1.30 (m, 4H); 0.90 (dd, $J=7.2$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3); δ (ppm): 173.9, 152.9, 137.2, 129.3 (2C), 128.9 (2C), 127.0, 82.3, 63.7, 35.9, 35.6, 31.5, 28.8, 24.3, 22.7, 22.5, 14.2. LRMS (ESI) calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 326.1732, found 326.18.

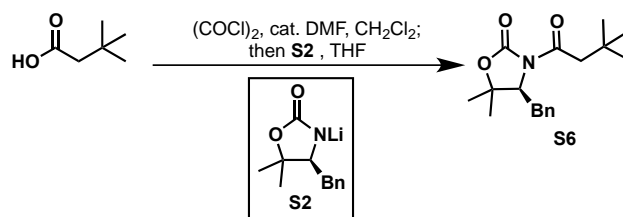


(S)-4-Benzyl-5,5-dimethyl-3-(3-methylbutanoyl)oxazolidin-2-one (3.32). The title compound was prepared from commercially available isovaleric acid (1.09 mL, 10.0 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a colorless oil (1.29 g, 4.46 mmol, 45%) after purification by column chromatography (silica, 10% ethyl acetate - hexanes). α_D^{24} -31.8° (c 1.0, dichloromethane).

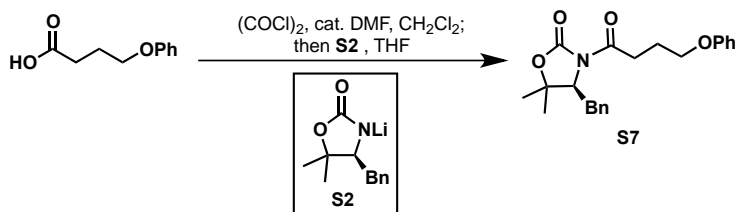
^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.32-7.26 (m, 4H); 7.24-7.20 (m, 1H); 4.52 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 3.14 (dd, $J_1=14.4$ Hz, $J_2=3.6$ Hz, 1H); 2.88 (dd, $J_1=14.4$ Hz, $J_2=9.6$ Hz, 1H); 2.85-2.78 (m, 2H); 2.19-2.12 (m, 1H); 1.36 (s, 3H); 1.35 (s, 3H); 0.97 (d, $J=7.2$ Hz, 3H); 0.96 (d, $J=7.2$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 173.1, 152.8, 137.2, 129.3 (2C), 128.9 (2C), 127.0, 82.2, 63.7, 44.3, 35.6, 28.7, 25.4, 22.7, 22.6, 22.5. LRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 312.1576, found 312.17.



(*S*)-4-Benzyl-3-(2-cyclohexylacetyl)-5,5-dimethyloxazolidin-2-one (3.33). The title compound was prepared from commercially available cyclohexanecarboxylic acid (0.710 g, 5.00 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a white solid (1.00 g, 3.04 mmol, 61%) after purification by column chromatography (silica, 10% ethyl acetate - hexanes). $\alpha_{\text{D}}^{24} -31.5^\circ$ (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.32-7.25 (m, 4H); 7.24-7.20 (m, 1H); 4.51 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 3.13 (dd, $J_1=14.4$ Hz, $J_2=3.6$ Hz, 1H); 2.88 (dd, $J_1=14.4$ Hz, $J_2=9.6$ Hz, 1H); 2.81 (ddd, $J_1=22.8$ Hz, $J_2=15.6$ Hz, $J_3=7.2$ Hz, 2H); 1.88-1.79 (m, 1H); 1.73-1.62 (m, 5H); 1.36 (s, 3H); 1.35 (s, 3H); 1.32-1.22 (m, 2H); 1.19-1.10 (m, 1H); 1.05-0.95 (m, 2H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 173.1, 152.9, 137.2, 129.3 (2C), 128.9 (2C), 127.0, 105.2, 82.2, 63.7, 42.9, 35.7, 34.7, 33.3, 33.2, 28.8, 26.4, 26.3, 22.5. LRMS (ESI) calcd for $\text{C}_{20}\text{H}_{27}\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 352.1889, found 352.20.

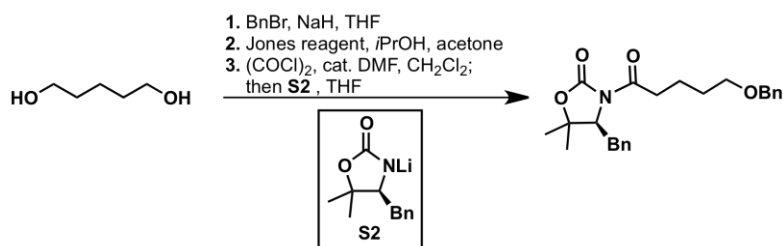


(S)-4-Benzyl-3-(3,3-dimethylbutanoyl)-5,5-dimethyloxazolidin-2-one (3.34). The title compound was prepared from commercially available 3,3-dimethylbutyric acid (1.27 mL, 10.0 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a colorless oil (1.74 g, 5.74 mmol, 57%) after purification by column chromatography (silica, 10% ethyl acetate - hexanes). α_D^{23} -28.8° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.32-7.27 (m, 4H); 7.24-7.21 (m, 1H); 4.55 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 3.17 (dd, $J_1=13.8$ Hz, $J_2=3.6$ Hz, 1H); 2.96-2.83 (m, 3H); 1.35 (s, 6H); 1.05 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 172.4, 152.9, 137.3, 129.2 (2C), 128.9 (2C), 127.0, 81.8, 63.8, 46.5, 35.6, 31.8, 29.9 (3C), 28.8, 22.6. LRMS (ESI) calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{Na}$ [M+Na] 326.1732, found 326.18.



(S)-4-Benzyl-5,5-dimethyl-3-(4-phenoxybutanoyl)oxazolidin-2-one (3.35). The title compound was prepared from commercially available 4-phenoxybutanoic acid (1.80 g, 10.0 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a yellowish oil (1.55 g, 4.22 mmol, 42%) after purification by column chromatography (silica, 30% ethyl acetate - hexanes). α_D^{22} -27.0° (c 1.0, dichloromethane).

^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.30-7.24 (m, 6H); 7.22-7.20 (m, 1H); 6.95-6.92 (m, 1H); 6.90-6.88 (m, 2H); 4.52 (dd, $J_1=9.6$ Hz, $J_2=4.8$, 1H); 4.04-3.95 (m, 2H); 3.16-3.10 (m, 3H); 2.88 (dd, $J_1=13.8$ Hz, $J_2=9.0$ Hz, 1H); 2.16-2.07 (m, 2H); 1.38 (s, 3H); 1.36 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 173.1, 159.0, 152.9, 137.1, 129.6 (2C), 129.3 (2C), 128.9 (2C), 127.0, 120.9, 114.7 (2C), 82.5, 66.7, 63.7, 35.7, 32.6, 28.7, 24.2, 22.5. LRMS (ESI) calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_4\text{Na}$ [$\text{M}+\text{Na}$] 390.1681, found 390.17.



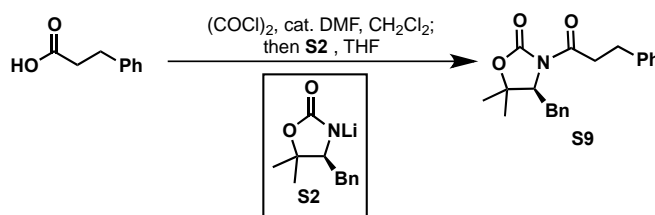
(S)-4-Benzyl-3-(5-(benzyloxy)pentanoyl)-5,5-dimethyloxazolidin-2-one (3.36). A solution of 1,5-pentanediol (1.60 mL, 15.2 mmol) in THF (3.20 mL) was added to a slurry of sodium hydride (60wt% in mineral oil, 0.104 g, 2.62 mmol) in THF (6.39 mL) over 30 min at 0 °C. After stirring for an additional 30 min, a solution of benzyl bromide (0.260 mL, 2.18 mmol) in THF (3.21 mL) was added to the reaction mixture over 30 min. The reaction mixture was then warmed to rt and stirred an additional 20 h. The reaction was quenched with water, and THF was removed *in vacuo*. The aqueous layer was extracted with ethyl acetate (3x20 mL). The combined organic layers were washed with water (6x20 mL), dried with sodium sulfate, and concentrated *in vacuo*. The resulting oil was submitted to the next reaction without further purification.

The crude mono-protected alcohol (0.517 g, 2.66 mmol) was dissolved in acetone (14.8 mL) and cooled to 0 °C. Jones reagent (3.35 M in water, 1.98 mL, 6.65 mmol) was added

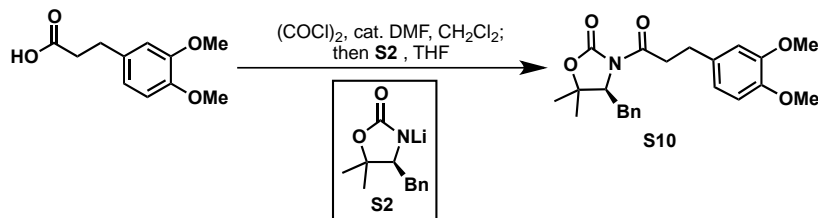
dropwise over 20 min. After 1 h at 0 °C, isopropanol (3.8 mL) was added to the reaction mixture. After 30 min at 0 °C, solid sodium bicarbonate was added until the reaction mixture was neutral (pH ~ 7). The reaction mixture was filtered through Celite and the solids were washed with acetone and diethyl ether. The solution was concentrated *in vacuo*. Solid sodium hydroxide was added to the resulting aqueous solution until basic (pH ~ 12). The aqueous layer was extracted with diethyl ether (3x20 mL). Concentrated HCl (12 M) was then added to the aqueous layer until acidic (pH ~ 1). The aqueous layer was extracted with diethyl ether (3x20 mL). The combined organic layers were dried with sodium sulfate and concentrated *in vacuo*. The resulting white solid was submitted to the next reaction without further purification.

Oxalyl chloride (0.660 mL, 0.770 mmol) was added to a solution of the crude carboxylic acid (0.146 g, 0.700 mmol), dimethylformamide (about 10 µl), and dichloromethane (0.470 mL) at 0 °C. After 10 min, the solution was warmed to rt and stirred an additional 15 min (until all bubbling had stopped). The solution was concentrated *in vacuo*. In a separate flask, *n*-butyllithium (2.43 M in hexanes, 0.200 mL, 0.490 mmol), was added to a solution of oxazolidinone **S1** (94.0 mg, 0.460 mmol) in THF (1.20 mL) at -78 °C under argon. The solution was stirred for 30 min at -78 °C then the crude acid chloride in THF (1.30 mL total with rinses) was added dropwise at -78 °C. After 2 h, the reaction mixture was warmed to 0 °C over 30 min and was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The desired compound **S8** was obtained as a yellowish oil (0.123 g, 0.311 mmol, 44% over 3 steps) after purification

by column chromatography (silica, 30% ethyl acetate – hexanes). α_D^{24} -20.8° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.34-7.22 (m, 10H); 4.52-4.47 (m, 3H); 3.50 (dd, $J_1=J_2=6.0$ Hz, 2H); 3.13 (dd, $J_1=11.4$ Hz, $J_2=3.6$ Hz, 1H); 3.00-2.89 (m, 2H); 2.85 (dd, $J_1=13.8$ Hz, $J_2=9.0$ Hz, 1H); 1.77-1.71 (m, 2H); 1.70-1.64 (m, 2H); 1.36 (s, 3H); 1.34 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 173.5, 152.9, 138.8, 137.2, 129.3 (2C), 128.7 (2C), 128.6 (2C), 127.9 (2C), 127.7, 127.0, 82.4, 73.1, 70.2, 63.7, 35.60, 35.59, 29.3, 28.8, 22.5, 21.3. LRMS (ESI) calcd for $\text{C}_{24}\text{H}_{29}\text{NO}_4\text{Na}$ [$\text{M}+\text{Na}$] 418.1994, found 418.21.

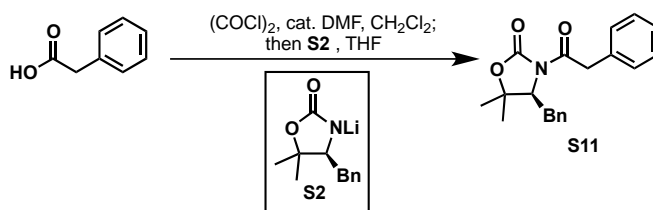


(S)-4-Benzyl-5,5-dimethyl-3-(3-phenylpropanoyl)oxazolidin-2-one (3.37). The title compound was prepared from commercially available hydrocinnamic acid (1.50 g, 10.0 mmol) following the standard procedure for the synthesis of *N*-acyl oxazolidinones and was obtained as a white solid (1.74 g, 5.16 mmol, 52%) after purification by column chromatography (silica, 20% ethyl acetate - hexanes). α_D^{24} -21.7° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.32-7.18 (m, 10H); 4.50 (dd, $J_1=9.6$ Hz, $J_2=4.2$ Hz, 1H); 3.31-3.21 (m, 2H); 3.13 (dd, $J_1=14.4$ Hz, $J_2=4.2$ Hz, 1H); 3.01-2.92 (m, 2H); 2.86 (dd, $J_1=14.4$ Hz, $J_2=9.6$ Hz, 1H); 1.36 (s, 3H); 1.32 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 172.8, 152.8, 140.6, 137.1, 129.3 (2C), 128.9 (2C), 128.70 (2C), 128.66 (2C), 127.0, 126.4, 82.4, 63.7, 37.4, 35.5, 30.7, 28.7, 22.5. LRMS (ESI) calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 360.1576, found 360.16.



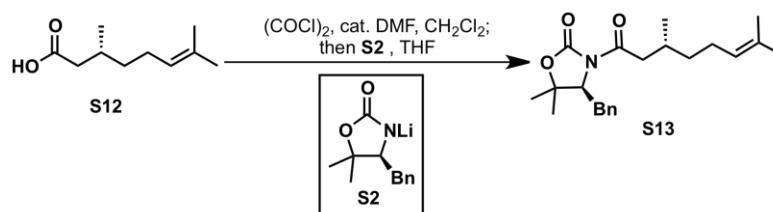
(S)-4-Benzyl-3-(3-(3,4-dimethoxyphenyl)propanoyl)-5,5-dimethyloxazolidin-2-one

(3.38). The title compound was prepared from commercially available 3-(3,4-dimethoxyphenyl)propanoic acid (2.10 g, 10.0 mol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a yellowish solid (2.37 g, 5.96 mmol, 60%) after purification by column chromatography (silica, 40% ethyl acetate - hexanes). α_D^{22} -17.3° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.31-7.20 (m, 5H); 6.80-6.76 (m, 3H); 4.49 (dd, $J_1=10.2$ Hz, $J_2=4.2$ Hz, 1H); 3.87 (s, 3H); 3.85 (s, 3H); 3.29-3.19 (m, 2H); 3.11 (dd, $J_1=14.4$ Hz, $J_2=4.2$ Hz, 1H); 2.94-2.87 (m, 2H); 2.85 (dd, $J_1=14.4$ Hz, $J_2=10.2$ Hz, 1H); 1.36 (s, 3H); 1.31 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 172.9, 152.8, 149.1, 147.7, 137.1, 133.2, 129.3 (2C), 128.9 (2C), 127.0, 120.6, 112.0, 114.5, 82.5, 63.7, 56.2, 56.0, 37.6, 35.5, 30.4, 28.7, 22.5. LRMS (ESI) calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_5\text{Na}$ [M+Na] 420.1787, found 420.18.



(S)-4-Benzyl-5,5-dimethyl-3-(2-phenylacetyl)oxazolidin-2-one (3.39). The title compound was prepared from commercially available phenylacetic acid (0.681 g, 5.00

mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a white solid (0.788 g, 2.44 mmol, 49%) after purification by column chromatography (silica, 20% ethyl acetate - hexanes). $\alpha_D^{24} -21.5^\circ$ (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.35-7.31 (m, 2H); 7.31-7.19 (m, 8H); 4.50 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 4.28 (AB, $J_A=18.6$ Hz, $J_B=15.6$ Hz, 2H); 3.14 (dd, $J_1=13.8$ Hz, $J_2=3.6$ Hz, 1H); 2.86 (dd, $J_1=13.8$ Hz, $J_2=9.6$ Hz, 1H); 1.36 (s, 3H); 1.32 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 171.7, 152.8, 137.0, 133.9, 129.9 (2C), 129.3 (2C), 128.9 (2C), 128.8 (2C), 127.4, 127.0, 85.6, 64.0, 42.0, 35.4, 28.8, 22.5. LRMS (ESI) calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]$ 346.1419, found 346.15.

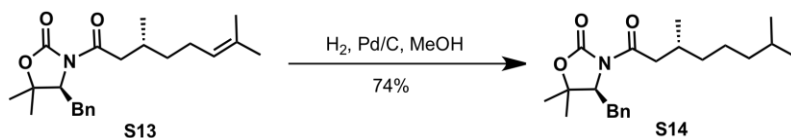


(S)-4-Benzyl-3-((R)-3,7-dimethyloct-6-enoyl)-5,5-dimethyloxazolidin-2-one (3.40).

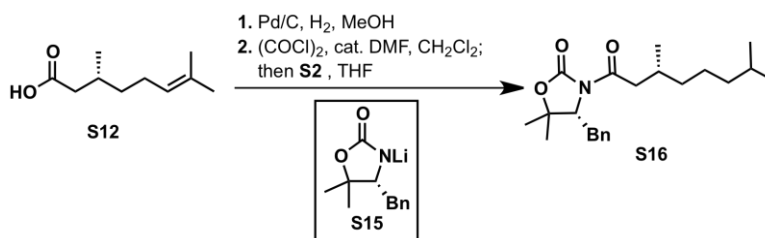
The title compound was prepared from (R)-(+)-citronellic acid **S14** (5.88 g, 16.5 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as a colorless oil (4.82 g, 13.5 mmol, 82%) after purification by column chromatography (silica, 20% ethyl acetate - hexanes). $\alpha_D^{22} -21.4^\circ$ (c 10.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.32-7.26 (m, 4H); 7.25-7.20 (m, 1H); 5.11-5.06 (m, 1H); 4.52 (dd, $J_1=9.0$ Hz, $J_2=3.6$ Hz, 1H); 3.15 (dd, $J_1=14.4$ Hz, $J_2=3.6$ Hz, 1H); 2.93-2.84 (m, 2H); 2.79 (dd, $J_1=16.8$ Hz, $J_2=7.8$ Hz, 1H); 2.08-1.92 (m, 3H); 1.67 (s, 3H), 1.59 (s, 3H); 1.42-1.35 (m, 1H); 1.36 (s, 3H); 1.35 (s, 3H); 1.28-1.20 (m, 1H); 0.93 (d, $J=6.6$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 173.2, 152.7, 137.2, 131.7, 129.3 (2C), 128.9

(2C), 127.0, 124.6, 82.2, 63.7, 42.7, 37.0, 35.6, 29.7, 28.8, 25.9, 25.7, 22.5, 19.8, 17.9.

LRMS (ESI) calcd for C₂₂H₃₁NO₃Na [M+Na] 380.2202, found 380.24.



(S)-4-Benzyl-3-((R)-3,7-dimethyloctanoyl)-5,5-dimethyloxazolidin-2-one (3.41). The substrate **3.40** (0.441 g, 1.23 mmol) and palladium on carbon (30.4 mg) were dissolved in methanol (6.83 mL). Hydrogen gas was bubbled through the reaction mixture for 2 min at room temp. The reaction mixture flask was pressurized with hydrogen and the reaction was stirred for 1 h at rt. The reaction mixture was filtered through Celite and the solvent was removed *in vacuo* to afford the desired product (0.476 g, 1.33 mmol, 74%). α_D^{23} -21.5° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 7.32-7.25 (m, 4H); 7.25-7.20 (m, 1H); 4.52 (dd, J1=9.6 Hz, J2=4.2 Hz, 1H); 3.15 (dd, J1=14.4 Hz, J2=4.2 Hz, 1H); 2.94-2.84 (m, 2H); 2.75 (dd, J1=15.6 Hz, J2=7.8 Hz, 1H); 2.06-1.98 (m, 1H); 1.57-1.50 (m, 1H); 1.36 (s, 3H); 1.35 (s, 3H); 1.35-1.12 (m, 6H); 0.92 (d, J=6.6 Hz, 3H); 0.862 (d, J=6.6 Hz, 3H); 0.859 (d, J=6.6 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 173.3, 152.9, 137.2, 129.3 (2C), 128.9 (2C), 127.0, 82.2, 63.7, 42.8, 39.3, 37.2, 35.6, 30.0, 28.8, 28.2, 24.9, 22.9, 22.8, 22.5, 19.9. LRMS (ESI) calcd for C₂₂H₃₃NO₃Na [M+Na] 382.2358, found 382.23.

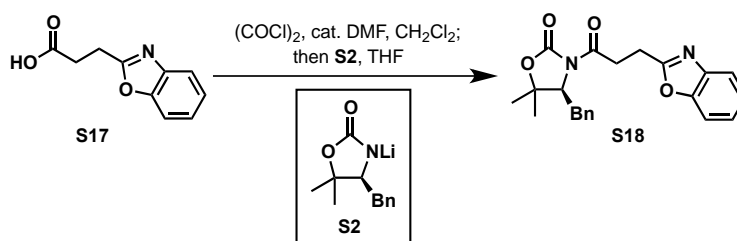


(R)-4-Benzyl-3-((R)-3,7-dimethyloct-6-enyl)-5,5-dimethyloxazolidin-2-one (3.42).

Oxalyl chloride (0.200 mL, 2.20 mmol) was added to a solution of (R)-(+)-citronellic acid (0.341 g, 2.00 mmol), dimethylformamide (10 μ L), and dichloromethane (1.00 mL) at 0 $^{\circ}$ C. After 10 min, the solution was warmed to rt and stirred an additional 15 min (until all bubbling had stopped). The solution was concentrated *in vacuo*. In a separate flask, *n*-butyllithium (2.39 M in hexanes, 0.880 mL, 2.10 mmol) was added to a solution of oxazolidinone (0.411 g, 2.00 mmol) in THF (4.00 mL) at -78 $^{\circ}$ C under argon. The solution was stirred for 30 min at -78 $^{\circ}$ C then the crude acyl chloride in THF (4.00 mL total with rinses) was added dropwise at -78 $^{\circ}$ C. After 2 h, the reaction mixture was warmed to 0 $^{\circ}$ C over 30 min and was quenched with saturated aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The resultant oil was submitted to the next reaction without further purification.

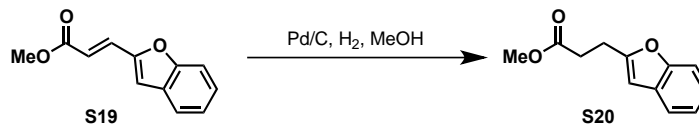
The crude substrate and palladium on carbon (48.0 mg) were dissolved in methanol (10.0 mL). Hydrogen gas was bubbled through the reaction mixture for 2 min at room temp. The reaction mixture flask was pressurized with hydrogen and the reaction was stirred for 3h at rt. The reaction mixture was filtered through Celite and the solvent was removed *in vacuo*. The desired compound **3.42** was obtained as an oil (0.406 g, 1.12 mmol, 56%) after purification by column chromatography (silica, 20% ethyl acetate - hexanes). α_D^{23} 22.1 $^{\circ}$ (c

1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 7.32-7.26 (m, 4H); 7.25-7.20 (m, 1H); 4.52 (dd, J₁=9.6 Hz, J₂=3.6 Hz, 1H); 3.15 (dd, J₁=14.4 Hz, J₂=3.6 Hz, 1H); 2.93-2.84 (m, 2H); 2.75 (dd, J₁=15.6 Hz, J₂=7.8 Hz, 1H); 2.07-1.97 (m, 1H); 1.56-1.48 (m, 1H); 1.36 (s, 3H); 1.35 (s, 3H); 1.35-1.11 (m, 6H); 0.93 (d, J=6.6 Hz, 3H); 0.87 (d, J=6.6 Hz, 3H); 0.86 (d, J=6.6 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 173.4, 152.9, 137.2, 129.3 (2C), 128.9 (2C), 127.0, 82.2, 63.7, 42.9, 39.3, 37.3, 35.6, 30.0, 28.7, 28.2, 24.9, 22.9, 22.8, 22.5, 19.9. LRMS (ESI) calcd for C₂₂H₃₃NO₃Na [M+Na] 382.2358, found 382.22.

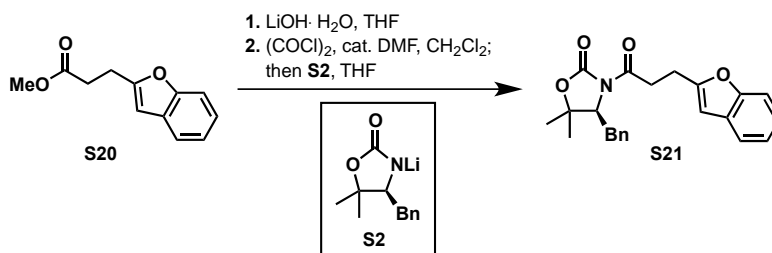


(S)-3-(3-(Benzo[d]oxazol-2-yl)propanoyl)-4-benzyl-5,5-dimethyloxazolidin-2-one

(3.44). The title compound was prepared from carboxylic acid **3.43** (0.471 g, 2.46 mmol)¹²² following the standard procedure for the synthesis of N-acyl oxazolidinones and was obtained as white solid (0.391 g, 1.03 mmol, 44%) after purification by column chromatography (silica, 25% ethyl acetate – hexanes, 40% ethyl acetate – hexanes). α_D²³ - 11.9° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 7.65-7.58 (m, 1H); 7.48-7.42 (m, 1H); 7.31-7.15 (m, 7H); 4.50 (dd, J₁=9.6 Hz, J₂=3.6 Hz, 1H); 3.66-3.55 (m, 1H); 3.54-3.42 (m, 1H); 3.33-3.18 (m, 2H); 3.14 (dd, J₁=14.4 Hz, J₂=3.6 Hz, 1H); 2.90 (dd, J₁=14.4 Hz, J₂=9.6 Hz, 1H); 1.39 (s, 3H); 1.37 (s, 3H). ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 171.7, 165.8, 152.8, 151.0, 141.5, 137.0, 129.2 (2C), 128.8 (2C), 127.0, 124.7, 124.3, 119.8, 110.5, 82.8, 63.7, 35.5, 32.6, 28.7, 23.4, 22.5. LRMS (ESI) calcd for C₂₂H₂₂N₂O₄Na [M+Na] 401.1477, found 401.14.



Methyl 3-(benzofuran-2-yl)propanoate (3.46). Crude α,β -unsaturated ester **3.45** (0.753 g, 3.42 mmol)¹²³ and palladium on carbon (75.3 mg) were dissolved in methanol (23.0 mL). Hydrogen was bubbled through the reaction mixture for 2 min at rt. The reaction mixture flask was pressurized with Hydrogen gas and the reaction was stirred for 1.5 h at rt. The reaction mixture was filtered through Celite and the solvent was removed *in vacuo*. The desired compound **3.46** was obtained as an oil (0.379 g, 1.86 mmol, 54%) after purification by column chromatography (silica, 5% ethyl acetate – hexanes, 10% ethyl acetate – hexanes, 15% ethyl acetate – hexanes). ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.50-7.46 (m, 1H); 7.43-7.39 (m, 1H); 7.24-7.16 (m, 2H); 6.43 (s, 1H); 3.71 (s, 3H); 3.12 (dd, J₁=J₂=7.8 Hz, 2H); 2.78 (dd, J₁=J₂=8.4 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃); δ (ppm): 172.9, 157.4, 154.9, 128.9, 123.7, 122.8, 120.6, 111.0, 102.7, 52.0, 32.3, 24.1. LRMS (ESI) calcd for C₁₂H₁₂O₃Na [M+Na] 227.0786, found 227.08.



(S)-3-(3-(Benzofuran-2-yl)propanoyl)-4-benzyl-5,5-dimethyloxazolidin-2-one (3.48).

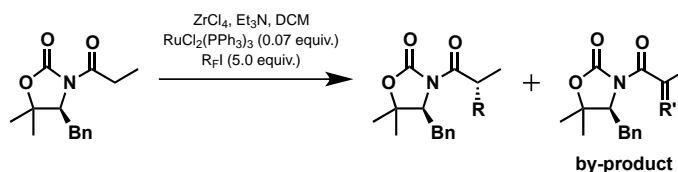
LiOH·H₂O (3.00 mL, 7.2 mmol, 2.42 M in water) was added to methyl ester **3.47** (0.367 g, 1.80 mmol) in THF (9.00 mL) at 0 °C. After 10 min the reaction mixture was warmed to rt

and stirred for 12 h. HCl (1 M) was then added until the reaction mixture was acidic (pH ~ 4), and the layers were separated. The aqueous layer was extracted with ethyl acetate (3x20 mL). The combined organic layers were dried with sodium sulfate and concentrated. The resultant solid was submitted to the next reaction without further purification.

Oxalyl chloride (0.172 mL, 1.97 mmol) was added to a solution of the crude carboxylic acid (0.340 g, 1.79 mmol), dimethylformamide (10 μ L), and dichloromethane (1.80 mL) at 0 °C. After 10 min, the solution was warmed to rt and stirred an additional 15 min (until all bubbling had stopped). The solution was concentrated *in vacuo*. In a separate flask, *n*-butyllithium (2.10 M in hexanes, 0.895 mL, 1.88 mmol), was added to a solution of oxazolidinone (0.376 g, 1.83 mmol) in THF (3.60 mL) at -78 °C under argon. The solution was stirred for 30 min at -78 °C then the crude acid chloride in THF (3.60 mL total with rinses) was added dropwise at -78 °C. After 2 h, the reaction mixture was warmed to 0 °C over 30 min and was quenched with saturated aqueous ammonium chloride. The layers were separated. The aqueous layer was extracted with ethyl acetate (3x20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated. The desired compound **3.48** was obtained as a white solid (0.538 g, 1.43 mmol, 79%) after purification by column chromatography (silica, 15% ethyl acetate – hexanes, 30% ethyl acetate – hexanes). α_D^{23} -25.7° (c 1.63, CHCl₃). ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.50-7.46 (m, 1H); 7.43-7.38 (m, 1H); 7.32-7.24 (m, 4H); 7.24-7.15 (m, 3H); 6.45 (s, 1H); 4.53 (dd, J₁=9.6 Hz, J₂=4.2 Hz, 1H); 3.45-3.34 (m, 2H); 3.19-3.09 (m, 3H); 2.88 (dd, J₁=14.4 Hz, J₂=9.6 Hz, 1H); 1.38 (s, 3H), 1.36 (s, 3H); ¹³C NMR (150 MHz, CDCl₃); δ (ppm): 172.0, 157.5, 154.8, 152.8, 137.0, 129.2 (2C), 129.0, 128.8 (2C), 127.0, 123.5, 122.7, 120.6, 111.0, 102.8, 82.6, 63.7, 35.5, 34.0, 28.7, 23.3, 22.5. LRMS (ESI) calcd for C₂₃H₂₃NO₄Na [M+Na]

400.1525, found 400.11.

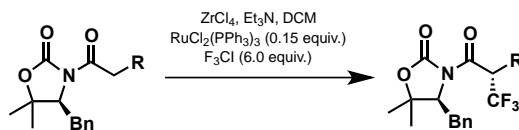
Standard procedure for perfluoralkylation of *N*-acyl oxazolidinones:



An *N*-acyl oxazolidinone (63.5 mg, 0.250 mmol), zirconium(IV) chloride (61.3 mg, 0.263 mmol, 1.05 equiv), and $\text{RuCl}_2(\text{PPh}_3)_3$ (16.8 mg, 0.0175 mmol, 0.07 equiv) were weighed out and added to a oven-dried vial equipped with a magnetic stir bar. Each reaction was capped with a black phenolic open-top screw cap lined with a white Silicone/TFE septum. The reaction vial was then backfilled with argon followed by addition of dry dichloromethane (2.50 mL) at rt. Triethylamine (0.122 mL, 0.875 mmol, 3.50 equiv) was added to the reaction mixture and stirred for 5 min, followed by addition of perfluoroalkyl iodide (1.25 mmol, 5.00 equiv). The vial cap was then replaced with a Teflon-lined cap. The reaction mixture was stirred for 1 h at rt, then heated to 45 °C and stirred for an additional 16 h. The sealed reaction vial was slowly opened (reaction is under pressure), and then added to HCl (1 M, 20 mL) in a separatory funnel. The layers were separated. The aqueous layer was extracted with dichloromethane (3x10 mL). The combined organic layers were dried with sodium sulfate, and concentrated on a rotary evaporator. The resulting compound was purified by column chromatography to give the corresponding α -perfluoralkylated oxazolidinone.

Alternative procedure for workup: The final reaction mixture can simply be filtered through a 1.5 cm plug of silica gel with ~ 1.0 cm of Celite on top washing with ethyl acetate. The filtrate is concentrated under reduced pressure to deliver the crude product.

Standard procedure for trifluoromethylation of *N*-acyl oxazolidinones:



For solid substrates: The *N*-acyl oxazolidinone (0.500 mmol), zirconium(IV) chloride (0.122 g, 0.525 mmol, 1.05 equiv), and $\text{RuCl}_2(\text{PPh}_3)_3$ (71.9 mg, 0.075 mmol, 0.15 equiv) were weighed out and added to a oven-dried vial equipped with a magnetic stir bar. Each reaction was capped with a black phenolic open-top screw cap lined with a white Silicone/TFE septum. The reaction vial was then backfilled with argon followed by addition of dry dichloromethane (1.00 mL) at rt. The reaction was cooled to $-78\text{ }^\circ\text{C}$, then triethylamine (0.280 mL, 2.00 mmol, 4.00 equiv) was added and the reaction was stirred for 5 min. Trifluoriodomethane (~0.230 mL, ~3.00 mmol, ~6.00 equiv) was then bubbled in via needle at $-78\text{ }^\circ\text{C}$. The vial cap was then replaced with a solid Teflon-lined cap. The reaction was warmed to rt and stirred for 1 h, then heated to $45\text{ }^\circ\text{C}$ and stirred for an additional 16 h. The sealed reaction vial was slowly opened (reaction is under pressure) until bubbling stopped, and then added to HCl (1 M, 20 mL) in a separatory funnel. The aqueous layer was extracted with dichloromethane (3x10 mL). The combined organic layers were dried with sodium sulfate, and concentrated on a rotary evaporator. The resulting compound was purified by column chromatography to give the corresponding α -trifluoromethylated *N*-acyl oxazolidinone.

Alternative procedure for workup: The final reaction mixture can simply be filtered through a 1.5 cm plug of silica gel with ~ 1.0 cm of Celite on top washing with ethyl acetate. The filtrate is concentrated under reduced pressure to deliver the crude product.

For liquid or amorphous substrates: Zirconium(IV) chloride (0.122 g, 0.525 mmol, 1.05 equiv) and $\text{RuCl}_2(\text{PPh}_3)_3$ (71.9 mg, 0.075 mmol, 0.15 equiv) were weighed out and added to a oven-dried vial equipped with a magnetic stir bar. Each reaction was capped with a black phenolic open-top screw cap lined with a white Silicone/TFE septum. The reaction vial was then backfilled with argon followed by addition of a solution of the *N*-acyl oxazolidinone (0.500 mmol) in dichloromethane (3 rinses, total of 1.00 mL) at rt. The reaction mixture was cooled to -78 °C, then triethylamine (0.280 mL, 2.00 mmol, 4.00 equiv) was added and the reaction was stirred for 5 min. Trifluoroiodomethane (~0.230 mL, ~3.00 mmol, ~6.00 eq.) was then bubbled in via needle at -78 °C. The vial cap was then replaced with a solid Teflon-lined cap. The reaction was warmed to rt and stirred for 1 h, then heated to 45 °C and stirred for an additional 16 h. The sealed reaction vial was slowly opened (reaction is under pressure) until bubbling stopped, and then added to HCl (1 M, 20 mL) in a separatory funnel. The aqueous layer was extracted with dichloromethane (3x10 mL). The combined organic layers were dried with sodium sulfate, and concentrated on a rotary evaporator. The resulting compound was purified by column chromatography to give the corresponding α -trifluoromethylated *N*-acyl oxazolidinone.

Alternative procedure for workup: The final reaction mixture can simply be filtered through a 1.5 cm plug of silica gel with ~ 1.0 cm of Celite on top washing with ethyl acetate. The filtrate is concentrated under reduced pressure to deliver the crude product.

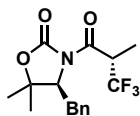


Table 3.4.2, entry 1. The title compound was prepared from oxazolidinone **3.12** (0.131 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.122 g, 0.370 mmol, 74%, dr 9:1) after purification by column chromatography (silica, 45% dichloromethane – hexanes, 15% ethyl acetate – hexanes, 20% ethyl acetate – hexanes). α_D^{25} 14.5° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.33-7.29 (m, 2H); 7.28-7.22 (m, 3H); 4.83 (app heptet, $J=7.8$ Hz, 1H); 4.53 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 3.19 (dd, $J_1=14.4$ Hz, $J_2=3.0$ Hz, 1H); 2.88 (dd, $J_1=14.4$ Hz, $J_2=9.6$ Hz, 1H); 1.44 (d, $J=7.2$ Hz, 3H); 1.40 (s, 3H); 1.34 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 168.6 (q, $J=2.9$ Hz), 152.3, 136.6, 129.2 (2C), 129.0 (2C), 127.2, 125.2 (q, $J=278.4$ Hz), 82.9, 64.2, 42.5 (q, $J=27.3$ Hz), 35.1, 28.8, 22.6, 11.4 (q, $J=2.9$ Hz). ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -69.15 (d, $J=7.9$ Hz, 3F). LRMS (ESI) calcd for $\text{C}_{16}\text{H}_{18}\text{F}_3\text{NO}_3\text{Na}$ [M+Na] 352.1136, found 352.13.

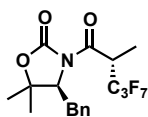


Table 3.4.2, entry 2. The title compound was prepared from oxazolidinone **3.12** (65.3 mg, 0.250 mmol) following the standard perfluoroalkylation procedure and was obtained as a colorless oil (79.0 mg, 0.185 mmol, 74%, dr 24:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 50% dichloromethane – hexanes). Analytically pure sample (white solid) was obtained using HPLC by dissolving the mixture in 0.5% *i*-ProH/hexanes with the concentration of 10

mg/ml. The separation was conducted on a YMC-Pack Sil HPLC column (250x30mmID, S-10 μ m, 12 nm) with 4.5 mL injection (0.25% *i*-PrOH/hexanes as eluent at a rate of 20 mL/min, λ =215 nm, R_t =14.55 min) afforded pure product. α_D^{25} -32.7° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.33-7.26 (m, 4H); 7.26-7.22 (m, 1H); 5.09 (app octet, J =7.2 Hz, 1H); 4.54 (dd, J_1 =10.8 Hz, J_2 =3.0 Hz, 1H); 3.25 (dd, J_1 =14.4 Hz, J_2 =3.0 Hz, 1H); 2.82 (dd, J_1 =14.4 Hz, J_2 =10.8 Hz, 1H); 1.48 (d, J =7.2 Hz, 3H); 1.38 (s, 3H); 1.32 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3); δ (ppm): 168.7 (t, J =3.3 Hz), 152.3, 136.8, 129.1 (2C), 129.0 (2C), 127.2, 121.8-105.0 (m, 3C), 82.8, 64.4, 39.3 (t, J =21.0 Hz), 34.7, 29.9, 28.9, 22.7, 11.4-11.2 (m, 1C). ^{19}F NMR (564.3 MHz, CDCl_3); δ (ppm): -80.59 (dd, J_1 = J_2 =10.2 Hz, 3F), -115.4 (m, 2F), -124.68 (m, 2F). LRMS (ESI) calcd for $\text{C}_{18}\text{H}_{18}\text{F}_7\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 452.1073, found 452.13.

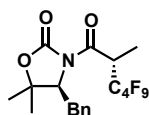


Table 3.4.2, entry 3. The title compound was prepared from oxazolidinone **3.12** (65.3 mg, 0.250 mmol) following the standard perfluoroalkylation procedure and was obtained as a colorless oil (85.4 mg, 0.178 mmol, 71%, dr 24:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 50% dichloromethane – hexanes). Analytically pure sample (white solid) was obtained using HPLC by dissolving the mixture in 0.5% *i*-PrOH/hexanes with the concentration of 10 mg/ml. The separation was conducted on a YMC-Pack Sil HPLC column (250x30mmID, S-10 μ m, 12 nm) with 4.5 mL injection (0.25% *i*-PrOH/hexanes as eluent at a rate of 20 mL/min, λ =215 nm, R_t =12.49 min) afforded pure product. α_D^{25} -24.3° (c 1.0,

dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.34-7.26 (m, 4H), 7.26-7.22 (m, 1H), 5.11 (app octet, $J=7.2$ Hz, 1H), 4.54 (dd, $J_1=10.2$ Hz, $J_2=3.0$ Hz, 1H), 3.24 (dd, $J_1=15.0$ Hz, $J_2=3.0$ Hz, 1H); 2.83 (dd, $J_1=15.0$ Hz, $J_2=10.2$ Hz, 1H); 1.48 (d, $J=7.2$ Hz, 3H); 1.38 (s, 3H); 1.33 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 168.8-168.6 (m, 1C), 152.3, 136.8, 129.2 (2C), 129.0 (2C), 127.2, 121.0-106.4 (m, 4C), 82.6, 64.4, 39.4 (t, $J=21.5$ Hz), 34.7, 28.8, 22.6, 11.5-11.3 (m, 1C). ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -80.91 (dd, $J=9.6$ Hz, 3F), -114.77 (m, 2F), -121.4 (m, 2F), -126.06 (m, 2F). LRMS (ESI) calcd for $\text{C}_{19}\text{H}_{18}\text{F}_9\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 502.1041, found 502.13.

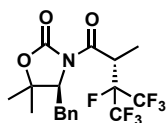


Table 3.4.2, entry 4. The title compound was prepared from oxazolidinone **3.12** (0.131 mg, 0.500 mmol) following the standard perfluoroalkylation procedure and was obtained as a colorless oil (0.161 g, 0.374 mmol, 75%, dr >98:2) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 50% dichloromethane – hexanes). α_D^{23} -17.2° (c 1.0, dichloromethane). ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.34-7.27 (m, 4H); 7.26-7.20 (m, 1H); 5.18 (dq, $J_d=14.5$ Hz, $J_q=7.5$ Hz, 1H); 4.53 (dd, $J_1=11.0$ Hz, $J_2=2.5$ Hz, 1H); 3.29 (dd, $J_1=14.5$ Hz, $J_2=2.5$ Hz, 1H); 2.76 (dd, $J_1=14.5$ Hz, $J_2=11.0$ Hz, 1H); 1.50 (d, $J=7.0$ Hz, 3H); 1.36 (s, 3H); 1.30 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 169.2 (d, $J=3.3$ Hz), 152.3, 136.8, 129.1 (2C), 129.0 (2C), 127.1, 120.98 (dq, $J=28.1$ Hz, $J=286.4$ Hz), 120.96 (dq, $J=28.1$ Hz, $J=286.4$ Hz), 92.4 (dh, $J=31.4$ Hz, $J=210.0$ Hz), 82.6, 64.5, 37.5 (d, $J=19.4$ Hz), 34.1, 28.7, 22.3, 12.4. ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -72.94 (dddd, $J=9.6$ Hz, 3F), -73.38 (dddd, $J=9.6$ Hz, 3F), -

182.04 (m, 1F). LRMS (ESI) calcd for C₁₈H₁₈F₇NO₃Na [M+Na] 452.1073, found 452.09.

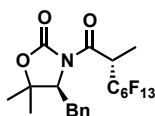


Table 3.4.2, entry 5. The title compound was prepared from oxazolidinone **3.12** (65.3 mg, 0.250 mmol) following the standard perfluoroalkylation procedure and was obtained as a white solid (93.0 mg, 0.159 mmol, 64%, dr >98:2) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 50% dichloromethane – hexanes). Analytically pure sample (white solid) was obtained using HPLC by dissolving the mixture in 0.5% *i*-ProH/hexanes with the concentration of 10 mg/ml. The separation was conducted on a YMC-Pack Sil HPLC column (250x30mmID, S-10 μ m, 12 nm) with 4.5 mL injection (0.25% *i*-PrOH/hexanes as eluent at a rate of 20 mL/min, λ =215 nm, R_t =14.65 min) afforded pure product. α_D^{25} -19.1° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.33-7.27 (m, 4H); 7.26-7.22 (m, 1H); 5.11 (app octet, J=7.2 Hz, 1H); 4.54 (dd, J₁=10.2 Hz, J₂=3.0 Hz, 1H); 3.25 (dd, J₁=14.4 Hz, J₂=3.0 Hz, 1H); 2.82 (dd, J₁=14.4 Hz, J₂=10.2 Hz, 1H); 1.48 (d, J=7.2 Hz, 3H); 1.38 (s, 3H); 1.33 (s, 3H); ¹³C NMR (150 MHz, CDCl₃); δ (ppm): 168.8-168.6 (m, 1C), 152.3, 136.8, 129.2 (2C), 129.0 (2C), 127.2, 120.5-106.4 (m, 6C), 82.7, 64.4, 39.4 (t, J=21.5 Hz), 34.7, 28.8, 22.6, 11.4. ¹⁹F NMR (564.3 MHz, CDCl₃); δ (ppm): -80.78 (dd, J₁=J₂=9.6 Hz, 3F), -114.52 (m, 2F), -120.36 (m, 2F), -121.91 (m, 2F), -122.72 (m, 2F), -126.09 (m, 2F). LRMS (ESI) calcd for C₂₁H₁₈F₁₃NO₃Na [M+Na] 602.0977, found 602.08.

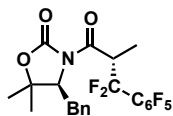


Table 3.4.2, entry 6. The title compound was prepared from oxazolidinone **3.12** (65.3 mg, 0.250 mmol) following the standard perfluoroalkylation procedure and was obtained as a white solid (87.4 mg, 0.183 mmol, 73%, dr >98:2) after purification by column chromatography (silica, 12.5% ethyl acetate – hexanes, 15% ethyl acetate – hexanes, 20% ethyl acetate – hexanes). Analytically pure sample (white solid) was obtained using HPLC by dissolving the mixture in 0.5% *i*-ProH/hexanes with the concentration of 10 mg/ml. The separation was conducted on a YMC-Pack Sil HPLC column (250x30mmID, S-10 μ m, 12 nm) with 4.5 mL injection (0.25% *i*-ProH/hexanes as eluent at a rate of 20 mL/min, λ =215 nm, R_t =13.44 min) afforded pure product. α_D^{23} -28.7° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.30-7.26 (m, 2H); 7.25-7.20 (m, 3H); 5.00 (app octet, J =6.6 Hz, 1H); 4.49 (dd, J_1 =10.2 Hz, J_2 =3.6 Hz, 1H); 3.14 (dd, J_1 =14.4 Hz, J_2 =3.6 Hz, 1H); 2.81 (dd, J_1 =14.4 Hz, J_2 =10.2 Hz, 1H); 1.45 (d, J =6.6 Hz, 3H); 1.37 (s, 3H); 1.33 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 169.9 (dd, J_1 =1.8 Hz, J_2 =6.2 Hz), 152.3, 146.0-144.0 (m, 2C), 143.6-141.6 (m, 1C), 139.0-137.0 (m, 2C), 136.7, 129.2 (2C), 128.9 (2C), 127.1, 119.5 (t, J =251.7 Hz), 110.3 (m, 1C), 82.9, 64.2, 45.8 (t, J =25.2 Hz), 34.8, 28.8, 22.5, 11.5 (t, J =4.5 Hz). ^{19}F NMR (564.3 MHz, CDCl_3); δ (ppm): -77.97 (dtd, J_{d1} =10.6 Hz, J_t =22.1 Hz, J_{d2} =232 Hz, 1F), -80.68 (dtd, J_{d1} =12.1 Hz, J_t =25.8 Hz, J_{d2} =232 Hz, 1F), -117.90 (m, 2F), -127.67 (t, J =17.5 Hz, 1F), 136.77 (m, 2F). LRMS (ESI) calcd for $\text{C}_{22}\text{H}_{18}\text{F}_7\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 500.1073, found 500.09.

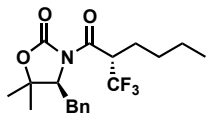


Table 3.4.3, entry 1. The title compound was prepared from oxazolidinone **3.31** (0.152 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.131 g, 0.353 mmol, 71%, dr ~9.4:1) after purification by column chromatography (silica, 40% dichloromethane – hexanes, 15% ethyl acetate – hexanes). α_D^{23} 6.8° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.33-7.25 (m, 4H); 7.25-7.21 (m, 1H); 4.99-4.89 (m, 1H); 4.56 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 3.15 (dd, $J_1=14.4$ Hz, $J_2=3.6$ Hz, 1H); 2.90 (dd, $J_1=14.4$ Hz, $J_2=9.6$ Hz, 1H); 2.04-1.95 (m, 1H); 1.87-1.79 (m, 1H); 1.39 (s, 3H); 1.42-1.25 (m, 4H); 1.35 (s, 3H); 0.90 (dd, $J_1=J_2=6.6$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 168.1 (q, $J=3.5$ Hz), 152.3, 136.7, 129.2 (2C), 128.9 (2C), 127.1, 125.0 (q, $J=279$ Hz), 82.7, 64.3, 47.0 (q, $J=26.3$ Hz), 35.2, 29.0, 28.7, 26.4 (q, $J=1.7$ Hz), 22.6, 22.4, 13.9. ^{19}F NMR (564.3 MHz, CDCl_3); δ (ppm): -67.11 (d, $J=7.9$ Hz, 3F). LRMS (ESI) calcd for $\text{C}_{19}\text{H}_{24}\text{F}_3\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 394.1606, found 394.17.

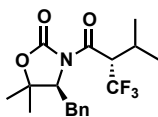


Table 3.4.3, entry 2. The title compound was prepared from oxazolidinone **3.32** (0.145 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.141 g, 0.395 mmol, 79%, dr >24:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 20% ethyl acetate – hexanes). α_D^{24} 5.4° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.33-7.27 (m, 4H); 7.25-7.21 (m, 1H), 4.82 (dq, $J_d=J_q=8.4$ Hz, 1H), 4.56

(dd, J1=10.2 Hz, J2=3.6 Hz, 1H), 3.16 (dd, J1=14.4 Hz, J2=3.6 Hz, 1H), 2.90 (dd, J1=14.4 Hz, J2=10.2 Hz, 1H), 2.47-2.37 (m, 1H), 1.37 (s, 3H), 1.36 (s, 3H), 1.14 (d, J=6.6 Hz, 3H), 1.03 (d, J=6.6 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 168.1 (q, J=3.9 Hz), 152.4, 136.8, 129.2 (2C), 128.9 (2C), 127.1, 125.1 (q, J=280.1 Hz), 82.5, 64.3, 52.9 (q, J=25.7 Hz), 35.1, 28.8, 28.1, 22.4, 20.8, 20.4. ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -63.03 (d, J=9.0 Hz, 3F). LRMS (ESI) calcd for $\text{C}_{18}\text{H}_{22}\text{F}_3\text{NO}_3\text{Na}$ [M+Na] 380.1449, found 380.15.

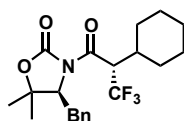


Table 3.4.3, entry 3. The title compound was prepared from oxazolidinone **3.33** (0.165 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.150 g, 0.378 mmol, 76%, dr >24:1) after purification by column chromatography (silica, 25% dichloromethane – hexanes, 35% dichloromethane – hexanes, 20% ethyl acetate – hexanes). α_D^{23} 19.3° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.34-7.27 (m, 4H); 7.25-7.21 (m, 1H); 4.88 (dq, $J_d=J_q=9.0$ Hz, 1H); 4.55 (dd, J1=10.2 Hz, J2=3.6 Hz, 1H); 3.16 (dd, J1=14.4 Hz, J2=3.6 Hz, 1H); 2.90 (dd, J1=14.4 Hz, J2=10.2 Hz, 1H); 2.18-2.09 (m, 1H); 2.01-1.95 (m, 1H); 1.81-1.69 (m, 2H); 1.69-1.60 (m, 2H); 1.37 (s, 3H); 1.36 (s, 3H); 1.33-1.24 (m, 2H); 1.22-1.15 (m, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 168.2 (q, J=3.9 Hz), 152.4, 136.9, 129.2 (2C), 128.9 (2C), 127.1, 125.1 (q, J=280.7 Hz), 82.5, 64.3, 52.3 (q, J=25.2 Hz), 37.2, 35.2, 30.7, 30.4, 28.8, 26.1, 25.9 (2C), 22.4. ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -62.32 (d, J=7.9 Hz, 3F). LRMS (ESI) calcd for $\text{C}_{21}\text{H}_{26}\text{F}_3\text{NO}_3\text{Na}$ [M+Na] 420.1762, found 420.18.

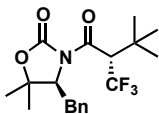


Table 3.4.3, entry 4. The title compound was prepared from oxazolidinone **3.34** (0.153 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.129 g, 0.348 mmol, 70%, dr >98:2) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes). α_D^{25} 90.9° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.33-7.29 (m, 4H); 7.26-7.21 (m, 1H); 5.10 (q, $J=9.0$ Hz, 1H); 4.57 (dd, $J_1=10.2$ Hz, $J_2=3.0$ Hz, 1H); 3.15 (dd, $J_1=14.4$ Hz, $J_2=3.0$ Hz, 1H); 2.90 (dd, $J_1=14.4$ Hz, $J_2=10.2$ Hz, 1H); 1.36 (s, 3H); 1.36 (s, 3H); 1.18 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 167.3 (q, $J=3.3$ Hz), 152.6, 136.9, 129.2 (2C), 128.9 (2C), 127.1, 125.4 (q, $J=281.3$ Hz), 82.3, 64.3, 53.8 (q, $J=24.6$ Hz), 35.2, 34.2, 28.9, 28.7 (3C), 22.4. ^{19}F NMR (564.3 MHz, CDCl_3); δ (ppm): -59.86 (d, $J=9.0$ Hz, 3F). LRMS (ESI) calcd for $\text{C}_{19}\text{H}_{24}\text{F}_3\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 394.1606, found 394.17.

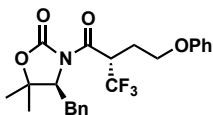


Table 3.4.3, entry 5. The title compound was prepared from oxazolidinone **3.35** (0.184 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.146 g, 0.336 mmol, 75%, dr 9:1) after purification by column chromatography (silica, 10% ethyl acetate – hexanes, 15% ethyl acetate – hexanes). α_D^{23} 42.8° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.34-7.29 (m, 2H); 7.29-7.21 (m, 5H); 6.94 (t, $J=7.2$ Hz, 1H); 6.86 (m, $J=8.4$ Hz, 2H); 5.41-5.31 (m, 1H); 4.51 (dd, $J_1=9.6$ Hz, $J_2=3.6$ Hz, 1H); 4.19-4.13 (m, 1H); 3.98-3.81 (m, 1H); 3.16 (dd, $J_1=14.4$

Hz, J2=3.6 Hz, 1H); 2.88 (dd, J1=14.4 Hz, J2=9.6 Hz, 1H); 2.56-2.48 (m, 1H); 2.35-2.28 (m, 1H); 1.33 (s, 3H); 1.05 (s, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 167.2 (q, J=3.3 Hz), 158.5, 152.2, 136.8, 129.7 (2C), 129.2 (2C), 128.9 (2C), 127.1, 125.1 (q, J=279.0 Hz), 121.6, 115.0 (2C), 82.6, 65.0, 64.3, 44.4 (q, J=27.3 Hz) 35.2, 28.3, 26.5-26.3 (m, 1C), 22.5. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -67.44 (d, J=7.9 Hz, 3F). LRMS (ESI) calcd for C₂₃H₂₄F₃NO₄Na [M+Na] 458.1555, found 458.18.

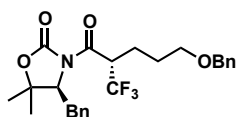


Table 3.4.3, entry 6. The title compound was prepared from oxazolidinone **3.36** (0.198 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.119 g, 0.256 mmol, 51%, dr 9:1) after purification by column chromatography (silica, 15% ethyl acetate – hexanes, 20% ethyl acetate – hexanes, 30% ethyl acetate – hexanes). α_D²³ 10.3° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 7.38-7.22 (m, 10H); 5.08-4.98 (m, 1H); 4.58-4.53 (m, 1H); 4.53-4.46 (m, 2H); 3.54-3.43 (m, 2H); 3.17 (dd, J1=14.4 Hz, J2=3.6 Hz, 1H); 2.90 (dd, J1=14.4 Hz, J2=10.2 Hz, 1H); 2.17-2.08 (m, 1H); 2.01-1.92 (m, 1H); 1.72-1.62 (m, 2H); 1.39 (s, 3H); 1.33 (s, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 167.8 (q, J=2.9 Hz), 152.2, 138.4, 136.7, 129.2 (2C), 128.9 (2C), 128.6 (2C), 127.9 (2C), 127.8, 127.1, 125.0 (q, J=280.7 Hz), 82.7, 73.2, 69.4, 64.2, 46.8, (q, J=26.9 Hz), 35.1, 28.6, 26.9, 23.7, 22.4. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -66.99 (d, J=7.9 Hz, 3F). LRMS (ESI) calcd for C₂₅H₂₈F₃NO₄Na [M+Na] 486.1868, found 486.17.

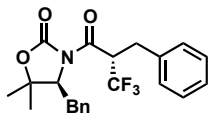


Table 3.4.3, entry 7. The title compound was prepared from oxazolidinone **3.37** (0.175 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.128 g, 0.315 mmol, 63%, dr 9.2:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 20% ethyl acetate – hexanes). α_D^{25} 96.0° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.31-7.25 (m, 4H); 7.25-7.18 (m, 6H); 5.45-5.36 (m, 1H); 4.25 (dd, $J_1=9.6$ Hz, $J_2=4.8$ Hz, 1H); 3.26-3.15 (m, 2H); 3.01 (dd, $J_1=15.0$ Hz, $J_2=4.8$ Hz, 1H); 2.85 (dd, $J_1=15.0$ Hz, $J_2=9.6$ Hz, 1H); 1.26 (s, 3H); 0.74 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 166.8 (q, $J=3.1$ Hz), 152.1, 136.6, 136.0, 129.4 (2C), 129.2 (2C), 129.0 (2C), 128.9 (2C), 127.5, 127.1, 124.6 (q, $J=279.6$ Hz), 82.7, 64.0, 48.1 (q, $J=26.3$ Hz), 35.5, 32.9 (q, $J=2.2$ Hz), 27.6, 22.2. ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -67.38 (d, $J=7.9$ Hz, 3F). LRMS (ESI) calcd for $\text{C}_{22}\text{H}_{22}\text{F}_3\text{NO}_3\text{Na}$ [$\text{M}+\text{Na}$] 428.1449, found 428.16.

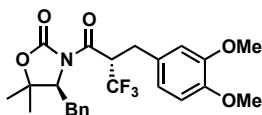


Table 3.4.3, entry 8. The title compound was prepared from oxazolidinone **3.38** (0.199 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.140 g, 0.300 mmol, 60%, dr 9:1) after purification by column chromatography (silica, 15% ethyl acetate – hexanes, 25% ethyl acetate – hexanes). α_D^{25} 90.9° (c 1.0, dichloromethane). ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.31-7.26 (m, 2H); 7.26-7.21 (m, 3H); 6.78-6.73 (m, 3H); 5.44 (app sextet, $J=7.2$ Hz, 1H); 4.26 (dd, $J_1=9.0$ Hz,

J2=4.2 Hz, 1H); 3.87 (s, 3H); 3.81 (s, 3H); 3.15 (d, J=7.8 Hz, 2H); 3.02 (dd, J1=14.4 Hz, J2=4.2 Hz, 1H); 2.87 (dd, J1=14.4 Hz, J2=9.0 Hz, 1H); 1.29 (s, 3H); 0.80 (s, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 166.8 (q, J=2.9 Hz), 152.2, 149.3, 148.4, 136.5, 129.2 (2C), 128.9 (2C), 128.2, 127.1, 124.6 (q, J=279.0 Hz), 121.4, 112.2, 111.6, 82.6, 64.0, 56.1 (2C), 47.9 (q, J=26.3 Hz), 35.5, 32.5 (q, J=2.3 Hz), 27.4, 22.1. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -67.31 (d, J=7.9 Hz, 3F). LRMS (ESI) calcd for C₂₄H₂₆F₃NO₅Na [M+Na] 488.1661, found 488.19.

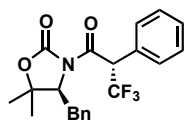


Table 3.4.3, entry 9. The title compound was prepared from oxazolidinone **3.39** (0.162 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (93.1 mg, 0.238 mmol, 48%, dr 8.4:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 20% ethyl acetate – hexanes). α_D²⁴ 24.3° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 7.50-7.46 (m, 2H); 7.40-7.36 (m, 3H); 7.34-7.27 (m, 4H); 7.27-7.23 (m, 1H); 5.90 (q, J=7.8 Hz, 1H); 4.44 (dd, J1=9.6 Hz, J2=3.6 Hz, 1H); 3.22 (dd, J1=14.4 Hz, J2=3.6 Hz, 1H); 2.96 (dd, J1=14.4 Hz, J2=9.6 Hz, 1H); 1.34 (s, 3H); 1.04 (s, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 166.0 (q, J=2.3 Hz), 152.0, 136.6 (2C), 130.4 (2C), 129.6, 129.3 (2C), 129.1 (2C), 129.0 (2C), 127.2, 124.0 (q, J=278.4 Hz), 83.1, 64.3, 53.1 (q, J=28.5 Hz), 35.5, 28.4, 22.2. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -66.71 (d, J=7.9 Hz, 3F). LRMS (ESI) calcd for C₂₁H₂₀F₃NO₃Na [M+Na] 414.1293, found 414.15.

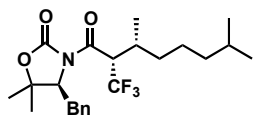


Table 3.4.3, entry 10. The title compound was prepared from oxazolidinone **3.41** (0.133 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.105 g, 0.245 mmol, 49%, dr 6.4:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 20% ethyl acetate – hexanes). α_D^{22} 11.7° (c 0.46, dichloromethane). ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.33-7.27 (m, 4H); 7.25-7.21 (m, 1H); 4.86 (dq, $J_d=J_q=8.4$ Hz, 1H); 4.56 (dd, $J_1=9.6$ Hz, $J_2=3.0$ Hz, 1H); 3.16 (dd, $J_1=15.0$ Hz, $J_2=3.0$ Hz, 1H); 2.90 (dd, $J_1=15.0$ Hz, $J_2=10.2$ Hz, 1H); 2.33-2.23 (m, 1H); 1.55-1.46 (m, 1H); 1.37 (s, 3H); 1.36 (s, 3H); 1.43-1.20 (m, 6H); 1.11 (d, $J=6.0$ Hz, 3H); 0.86 (d, $J=2.4$ Hz, 3H); 0.85 (d, $J=2.4$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); δ (ppm): 168.30-168.25 (m, 1C), 152.4, 136.8, 129.2 (2C), 129.0 (2C), 127.1, 125.1 (q, $J=280.8$ Hz), 82.6, 64.3, 52.3 (q, $J=26.3$ Hz), 39.1, 35.2, 34.8, 32.8, 28.8, 28.1, 24.5, 22.9, 22.7, 22.4, 16.6. ^{19}F NMR (564.3 MHz, CDCl_3); δ (ppm): -62.35 (d, $J=7.9$ Hz, 3F). LRMS (ESI) calcd for $\text{C}_{23}\text{H}_{32}\text{F}_3\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]$ 450.2232, found 450.20.

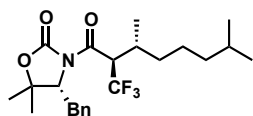


Table 3.4.3, entry 11. The title compound was prepared from oxazolidinone **3.42** (0.183 g, 0.500 mmol) following the standard trifluoromethylation procedure and was obtained as a colorless oil (0.113 g, 0.265 mmol, 53%, dr 10:1) after purification by column chromatography (silica, 35% dichloromethane – hexanes, 45% dichloromethane – hexanes, 20% ethyl acetate – hexanes). α_D^{22} -7.2° (c 1.0, dichloromethane). ^1H NMR (600 MHz, 20% ethyl acetate – hexanes).

CDCl₃); δ (ppm): 7.33-7.27 (m, 4H); 7.26-7.21 (m, 1H); 4.95 (dq, $J_d=J_q=8.4$ Hz, 1H); 4.55 (dd, $J_1=9.6$ Hz, $J_2=3.0$ Hz, 1H); 3.16 (dd, $J_1=15.0$ Hz, $J_2=3.0$ Hz, 1H); 2.91 (dd, $J_1=15.0$ Hz, $J_2=9.6$ Hz, 1H); 2.32-2.24 (m, 1H); 1.62-1.48 (m, 2H); 1.38 (s, 3H); 1.36 (s, 3H); 1.34-1.20 (m, 3H); 1.20-1.12 (m, 2H); 1.02 (d, $J=6.6$ Hz, 3H); 0.87 (d, $J=3.0$ Hz, 3H); 0.86 (d, $J=3.0$ Hz, 3H); ¹³C NMR (150 MHz, CDCl₃); δ (ppm): 168.0 (q, $J=3.5$ Hz), 152.4, 136.8, 129.2 (2C), 129.0 (2C), 127.1, 125.1 (q, $J=280.5$ Hz), 82.3, 64.1, 51.4 (q, $J=25.5$ Hz), 39.1, 35.2, 33.8, 32.7, 28.8, 28.1, 24.2, 22.9, 22.7, 22.4, 17.1. ¹⁹F NMR (564.3 MHz, CDCl₃); δ (ppm): -62.73 (d, $J=8.5$ Hz, 3F). LRMS (ESI) calcd for C₂₃H₃₂F₃NO₃Na [M+Na] 450.2232, found 450.24.

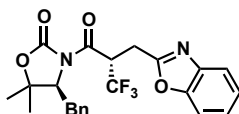
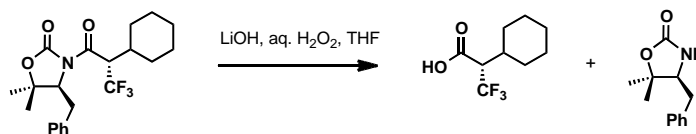


Table 3.4.3, entry 12. The title compound was prepared from oxazolidinone **3.44** (97.5 mg, 0.250 mmol) following the standard trifluoromethylation procedure (shorter reaction time: 4 h at 45 °C) with 0.20 equiv of RuCl₂(PPh₃)₃ (47.9 mg, 0.05 mmol) and was obtained as a colorless oil (37.5 mg, 0.084 mmol, 34%, dr 8.3:1) after purification by column chromatography (silica, 20% ethyl acetate – hexanes, 30% ethyl acetate – hexanes). Isomerically pure sample was obtained using HPLC by dissolving the mixture in 0.5% *i*-PrOH/hexanes with the concentration of 10 mg/ml. The separation was conducted on a YMC-Pack Sil HPLC column (250x30mmID, S-10 μ m, 12 nm) with 4.5 mL injection (0.25% *i*-PrOH/hexanes as eluent at a rate of 20 mL/min, $\lambda=215$ nm, $R_t=13.37$ min) affording pure product. α_D^{23} 36.1° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.50-7.45 (m, 2H); 7.32-7.20 (m, 7H); 5.74-5.66 (m, 1H); 4.57 (dd, $J_1=9.0$ Hz,

67.57 (d, J=8.5 Hz, 3F). LRMS (ESI) calcd for C₂₄H₂₂F₃NO₄Na [M+Na] 468.1399, found 468.10.

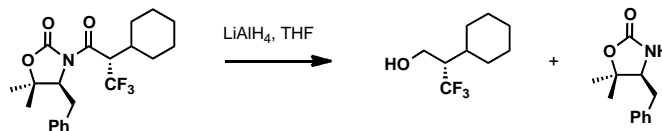


(S)-2-Cyclohexyl-3,3,3-trifluoropropanoic acid. Lithium hydroxide monohydrate (32 mg, 0.763 mmol) was added to a solution of the substrate (99.4 mg, 0.25 mmol), hydrogen peroxide (30%, 0.24 mL), and water (0.24 mL) in THF (1.00 mL) at 0 °C. The reaction was warmed to rt and stirred for 3 h, after which time H₂O (0.15 mL), H₂O₂ (0.15 mL), and LiOH·H₂O (30.0 mg) were added at rt and stirred for 3 h. The reaction was quenched with aqueous sodium sulfite (1.5 M) and HCl (1 M) and allowed to stir until two transparent layers were visible (pH ~4). The layers were separated and the aqueous layer was extracted with ethyl acetate (3x10 mL). The organic layer was then washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The crude material was then dissolved in ethyl acetate (5 mL) and extracted with aqueous sodium hydroxide (3 M, 3x5 mL) and water (2x5 mL). The aqueous extractions were combined and set aside. The organic layer was washed with HCl (1 M), brine, dried with sodium sulfate, and concentrated *in vacuo* to afford the oxazolidinone auxiliary (50.3 mg, 0.245 mmol, 98%). The previously saved aqueous layers were acidified with HCl (1 M). The aqueous layer was extracted with ethyl acetate (3x30 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated to afford the desired pure carboxylic acid (51.9 mg, 0.247 mmol, 99%). α_D^{21} 5.3° (c 1.0, dichloromethane). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 10.22-8.63 (bs, 1H); 2.98 (apparent pentet, J=8.5 Hz, 1H); 2.06-1.97 (m, 1H); 1.93-1.86 (m, 1H); 1.82-1.73 (m,

3H); 1.71-1.65 (m, 1H); 1.35-1.10 (m, 5H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 173.5 (m, 1C), 124.7 (q, $J=279.8$ Hz), 56.4 (q, $J=25.8$ Hz), 36.3, 31.0, 30.5, 26.1, 26.0, 25.9. ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -64.28 (d, $J=8.5$ Hz, 3F). LRMS (-ESI) calcd for $\text{C}_9\text{H}_{12}\text{F}_3\text{O}_2$ [M-H] 209.09, found 209.08.

Determination of er for the acid: A solution of the (*S*)-2-cyclohexyl-3,3,3-trifluoropropanoic acid in diethyl ether (0.2 M) was added to a solution of lithium aluminum hydride (4.0 equiv.) in diethyl ether (0.5 M) at -78°C and stirred for 15 min. The reaction mixture was warmed to rt over 1 h and then quenched using Feiser workup and allowed to stir for 2 h. The reaction mixture was filtered and concentrated *in vacuo*. No further purification was done.

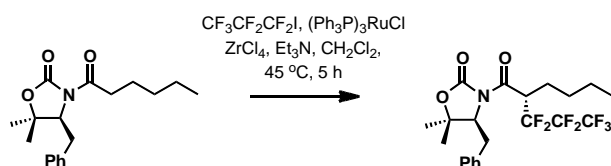
2-Naphthoyl chloride (2.0 equiv.) was added to a solution of the crude alcohol, triethylamine (2.0 equiv.), and 4-dimethylaminopyridine (0.1 equiv.) in dichloromethane (0.2 M) at 0°C . After 10 min, the reaction was warmed to rt and stirred for 30 min. The mixture was quenched with aqueous ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and purified by column chromatography (silica, 100% hexanes, 5% ethyl acetate – hexanes) to afford the desired naphthoyl ester derivative. HPLC analysis of the 2-naphthoyl ester derivative (OD-H, 2% Pr^iOH - hexanes, 1.0 mL/min, 254 nm) indicated er 97.2:2.8: R_T (major) = 6.8 minutes, R_T (minor) = 9.1 minutes.



(S)-2-Cyclohexyl-3,3,3-trifluoropropan-1-ol. A solution of the substrate (0.128 g, 0.322 mmol) in THF (1.10 mL total with rinses) was added to a solution of lithium aluminum hydride (22.1 mg, 0.582 mmol) in THF (0.58 mL) at -78 °C. After stirring 30 min, the reaction mixture was warmed to -50 °C and stirred an additional 30 min. The reaction mixture was quenched with water (23 µL) at -78 °C and stirred for 5 min. Then aqueous sodium hydroxide (3 M, 23 µL) was added at -78 °C and stirred for 5 min and warmed to rt. Then additional water (69 µL) was added and the reaction was stirred 2 h. The reaction mixture was filtered, concentrated *in vacuo*, and purified by column chromatography (silica, 15% EtOAc – Hexanes, 20% EtOAc – Hexanes, 40% EtOAc – Hexanes) to afford the desired alcohol (50.9 mg, 0.260 mmol, 81%) and the purified oxazolidinone (65.7 mg, 0.320 mmol, 99%). α_D^{21} -4.0° (c 1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 3.89 (dd, J₁=11.4 Hz, J₂=5.4 Hz, 1H); 3.82 (dd, J₁=11.4 Hz, J₂=4.2 Hz, 1H); 2.17-2.09 (m, 1H); 1.82-1.71 (m, 5H); 1.69-1.65 (m, 1H); 1.59 (bs, 1H); 1.30-1.20 (m, 3H); 1.19-1.10 (m, 2H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 128.5 (q, J=280.8 Hz), 59.0 (q, J=3.9 Hz), 51.2 (q, J=21.6 Hz), 35.7, 31.2, 29.9, 26.9, 26.8, 26.3. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -65.04 (d, J=10.2 Hz, 3F). FI calcd for C₉H₁₅F₃O [M] 196.11, found 196.11.

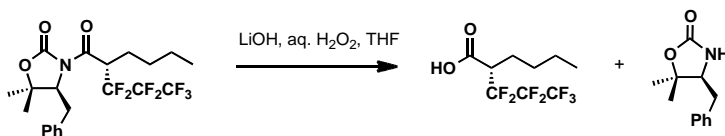
Determination of er for the alcohol: 2-Naphthoyl chloride (2.0 equiv.) was added to a solution of the crude alcohol substrate, triethylamine (2.0 equiv.), and 4-dimethylaminopyridine (0.1 equiv.) in dichloromethane (0.2 M) at 0 °C. After 10 min, the reaction was warmed to rt and stirred for 30 min. The reaction was quenched with aqueous

ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and purified by column chromatography (silica, 100% hexanes, 5% ethyl acetate – hexanes) to afford the desired naphthoyl ester derivative. HPLC analysis of the 2-naphthoyl ester derivative (OD-H, 2% PrⁱOH - hexanes, 1.0 mL/min, 254 nm) indicated er 99.2:0.8: R_T (major) = 6.5 minutes, R_T (minor) = 8.7 minutes.



Perfluoropropylation product 3.19: The title compound was prepared from oxazolidinone **3.31** (0.740 g, 2.44 mmol), zirconium(IV) chloride (0.597 g, 2.56 mmol), and RuCl₂(PPh₃)₃ (0.468 g, 0.488 mmol) following the standard perfluoroalkylation procedure (shorter reaction time: 5 h at 45 °C). The product was obtained as a an oil (0.750 g, 1.59 mmol, 65%, dr >98:2) along with recovered starting material (0.154 g, 0.510 mmol, 21%) after purification by column chromatography (silica, 15% ethyl acetate – hexanes, 20% ethyl acetate – hexanes). α_D^{23} 9.2° (c 1.0, CH₂Cl₂). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 7.33-7.29 (m, 4H); 7.25-7.21 (m, 1H), 5.24-5.15 (m, 1H); 4.58 (dd, J₁=10.8 Hz, J₂=3.0 Hz, 1H); 3.22 (dd, J₁=14.4 Hz, J₂=3.0 Hz, 1H); 2.84 (dd, J₁=14.4 Hz, J₂=10.8 Hz, 1H), 2.12-2.05 (m, 1H); 1.93-1.84 (m, 1H); 1.42-1.24 (m, 4H); 1.36 (s, 3H); 1.34 (s, 3H); 0.91 (dd, J=7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 168.2 (d, J=5.7 Hz), 152.3, 136.9, 129.1 (2C), 129.0 (2C), 127.1, 119.1-107.3 (m, 3C), 82.5, 64.5, 43.9 (m, 1C), 34.8, 28.9, 28.8, 26.0 (m, 1C), 22.6, 22.5, 13.9. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -80.55 (d, J=10.2

Hz, 3F); -113.99 (m, 2F); -127.70 (m, 2F). LRMS (ESI) calcd for C₂₄H₂₂F₃NO₄Na [M+Na] 494.06, found 494.06.

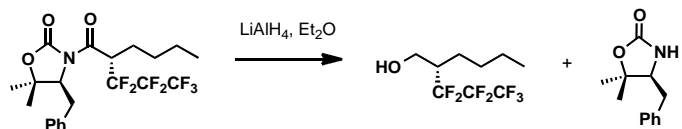


(S)-2-(Perfluoropropyl)hexanoic acid. Lithium hydroxide monohydrate (33.9 mg, 0.804 mmol) was added to a solution of the substrate (0.127 g, 0.269 mmol), hydrogen peroxide (30% in water, 0.40 mL), and water (0.40 mL) in THF (1.60 mL) at 0 °C and stirred for 10 min. The reaction was then warmed to rt and stirred for 3 h, after which additional H₂O (0.20 mL), H₂O₂ (0.20 mL), and LiOH·H₂O (30.0 mg) were added at rt and stirred for 2 h. The reaction was quenched with aqueous sodium sulfite (1.5 M) and HCl (1 M) and allowed to stir until two transparent layers were visible (pH ~4). The layers were separated and the aqueous layer was extracted with ethyl acetate (3x10 mL). The organic layer was then washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The crude material was then dissolved in ethyl acetate (5 mL) and extracted with aqueous sodium hydroxide (3 M, 3x5 mL) and water (2x5 mL). The aqueous extractions were combined and set aside. The organic layer was washed with HCl (1 M), brine, dried with sodium sulfate, and concentrated *in vacuo* to afford the oxazolidinone auxiliary (54.1 mg, 0.263 mmol, 98%). The previously saved aqueous layers were acidified with HCl (1 M). The aqueous layer was extracted with ethyl acetate (3x30 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo* to afford the desired carboxylic acid (65.4 mg, 0.230 mmol, 86%). α_D^{21} 9.5° (c 1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃); δ (ppm): 10.48 (bs, 1H); 3.22-2.13 (m, 1H); 2.01-1.93 (m, 1H); 1.92-1.84 (m, 1H);

1.45-1.32 (m, 4H); 0.93 (dd, $J_1=J_2=6.6$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3); $\delta(\text{ppm})$: 174.0 (d, $J=8.0$ Hz), 121.0-107.2 (m, 3C), 48.1 (t, $J=20.7$ Hz), 29.1, 25.0, 22.4, 13.8. ^{19}F NMR (564.3 MHz, CDCl_3); $\delta(\text{ppm})$: -80.59 (dd, $J=11.3$ Hz, 3F), -115.52 (m, 2F), -125.45 (m, 2F). FI calcd for $\text{C}_9\text{H}_{11}\text{F}_7\text{O}_2$ [M] 284.06, found 284.06.

Determination of er for the acid: A solution of the substrate in diethyl ether (0.2 M) was added to a solution of lithium aluminum hydride (4.0 equiv.) in diethyl ether (0.5 M) at -78 °C and stirred for 15 min. The reaction was warmed to rt over 1 h then the reaction was quenched using Feiser workup and allowed to stir for 2 h. The reaction mixture was filtered and concentrated *in vacuo*. No further purification was done.

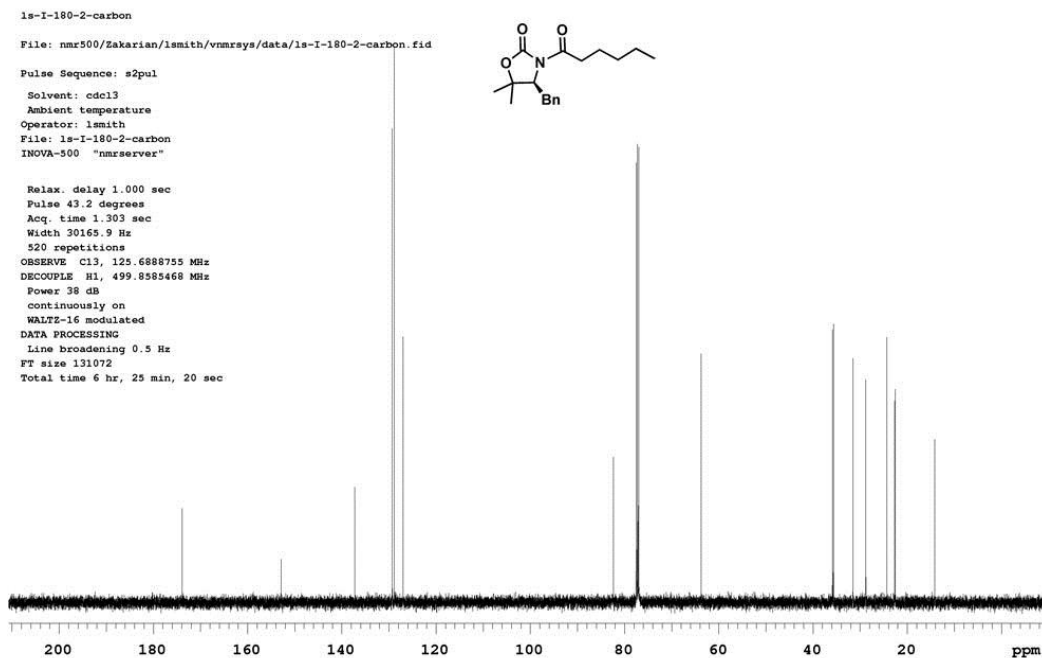
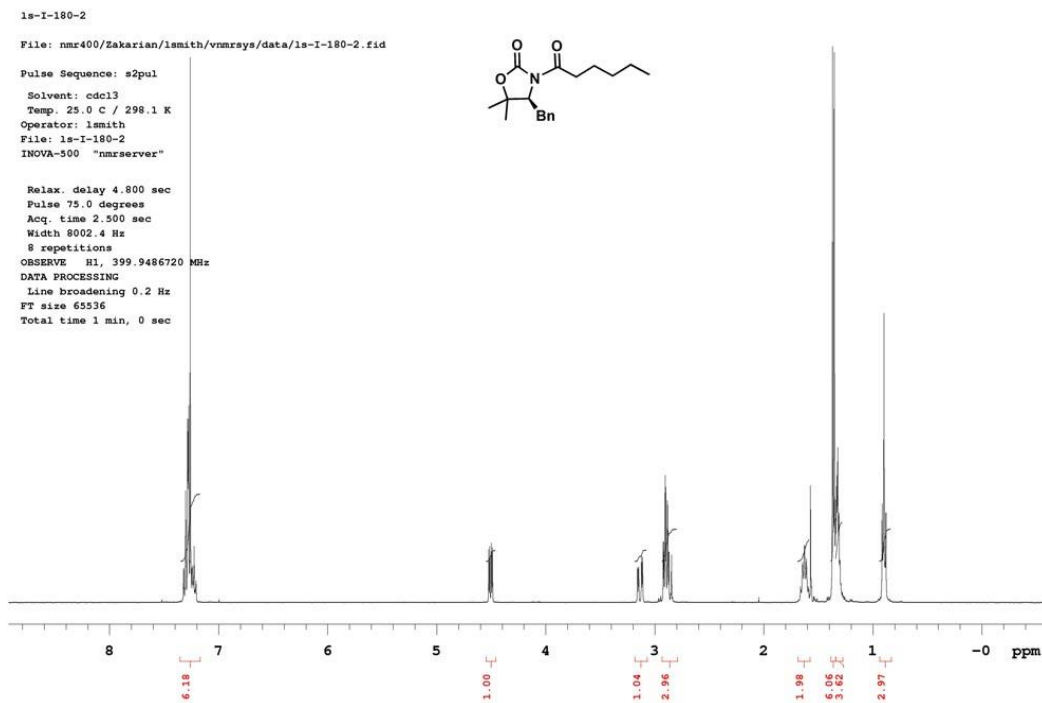
2-Naphthoyl chloride (2.0 equiv.) was added to a solution of the crude alcohol substrate, triethylamine (2.0 equiv.), and 4-dimethylaminopyridine (0.1 equiv.) in dichloromethane (0.2 M) at 0 °C. After 10 min, the reaction was warmed to rt and stirred for 30 min. The reaction was quenched with aqueous ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and purified by column chromatography (silica, 100% hexanes, 5% ethyl acetate – hexanes) to afford the desired naphthoyl ester derivative. HPLC analysis of the 2-naphthoyl ester derivative (OD-H, 0.5% Pr^iOH - hexanes, 1.0 mL/min, 254 nm) indicated er 98.1:1.9: R_T (major) = 7.6 minutes, R_T (minor) = 11.2 minutes.



(S)-2-(Perfluoropropyl)hexan-1-ol. A solution of the substrate (0.150 g, 0.318 mmol) in diethyl ether (1.60 mL total with rinses) was added to a solution of lithium aluminum hydride (24.3 mg, 0.640 mmol) in Et₂O (1.28 mL) at -78 °C and stirred for 30 min. Feiser workup: The reaction was quenched with water (24 µL) at -78 °C and stirred for 5 min. Then aqueous sodium hydroxide (3 M, 24 µL) was added at -78 °C and stirred for 5 min and warmed to rt. Then additional water (72 µL) was added and the reaction was stirred 2h. The reaction mixture was filtered, concentrated *in vacuo*, and purified by column chromatography (silica, 15% Et₂O – Pentane, 25% Et₂O – Pentane, 50% Et₂O – Pentane) to afford a mixture of the alcohol and allylic alcohol (76.9 mg, 0.286 mmol, 90%, containing 6% allylic alcohol) and the purified auxiliary (65.0 mg, 0.317 mmol, 99%). α_D^{21} 3.8° (c 1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃); δ(ppm): 3.93-3.84 (m, 2H); 2.34-2.24 (m, 1H); 1.74-1.67 (m, 1H); 1.67-1.57 (m, 2H); 1.52-1.45 (m, 1H); 1.40-1.31 (m, 3H); 0.93 (dd, J=7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃); δ(ppm): 121.2-107.7 (m, 3C), 59.2 (dd, J=5.9 Hz), 43.9 (dd, J=18.5 Hz), 29.4, 23.8-23.7 (m), 22.8, 14.0. ¹⁹F NMR (564.3 MHz, CDCl₃); δ(ppm): -80.76 (m, 3F), -114.74 (m, 2F), -125.36 (m, 2F). FI calcd for C₉H₁₄F₇O [M+H] 271.09, found 271.10.

Determination of er for the alcohol: 2-Naphthoyl chloride (2.0 equiv.) was added to a solution of the crude alcohol substrate, triethylamine (2.0 equiv.), and 4-dimethylaminopyridine 0.1 equiv.) in dichloromethane (0.2 M) at 0 °C. After 10 min, the reaction was warmed to rt and stirred for 30 min. The reaction was quenched with aqueous

ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3x10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and purified by column chromatography (silica, 100% hexanes, 5% ethyl acetate – hexanes) to afford the desired naphthoyl ester derivative. HPLC analysis of the 2-naphthoyl ester derivative (OD-H, 0.5% Pr^iOH - hexanes, 1.0 mL/min, 254 nm) indicated er 96.6:3.4: R_T (major) = 7.5 minutes, R_T (minor) = 11.0 minutes.



ls-I-250-2-2

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Pulse Sequence: s2pul

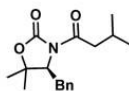
Solvent: cdcl3

Temp. 25.0 C / 298.1 K

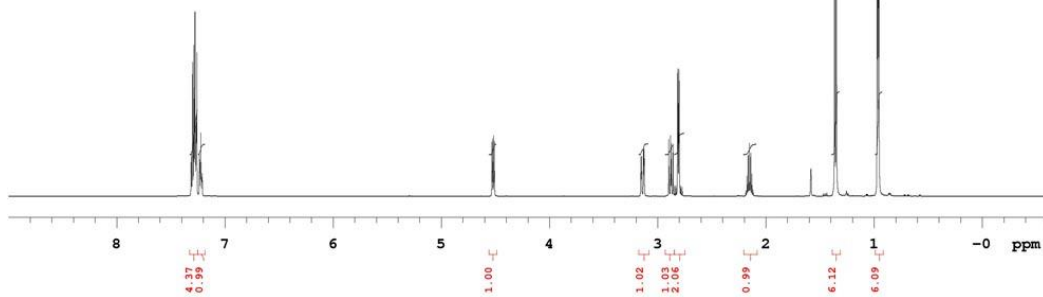
Operator: lsmith

File: ls-I-250-2-2

INOVA-500 "nmrserver"



Relax. delay 4.800 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6321124 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 0 min, 58 sec



ls-I-250-2-2-carbon

Sample: 1_Indanone

File: nmr600/Zakarian/lsmith/vmrsvs/data/ls-I-250-2-2-carbon.fid

Pulse Sequence: s2pul

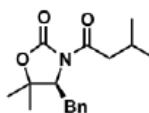
Solvent: cdcl3

Temp. 25.0 C / 298.1 K

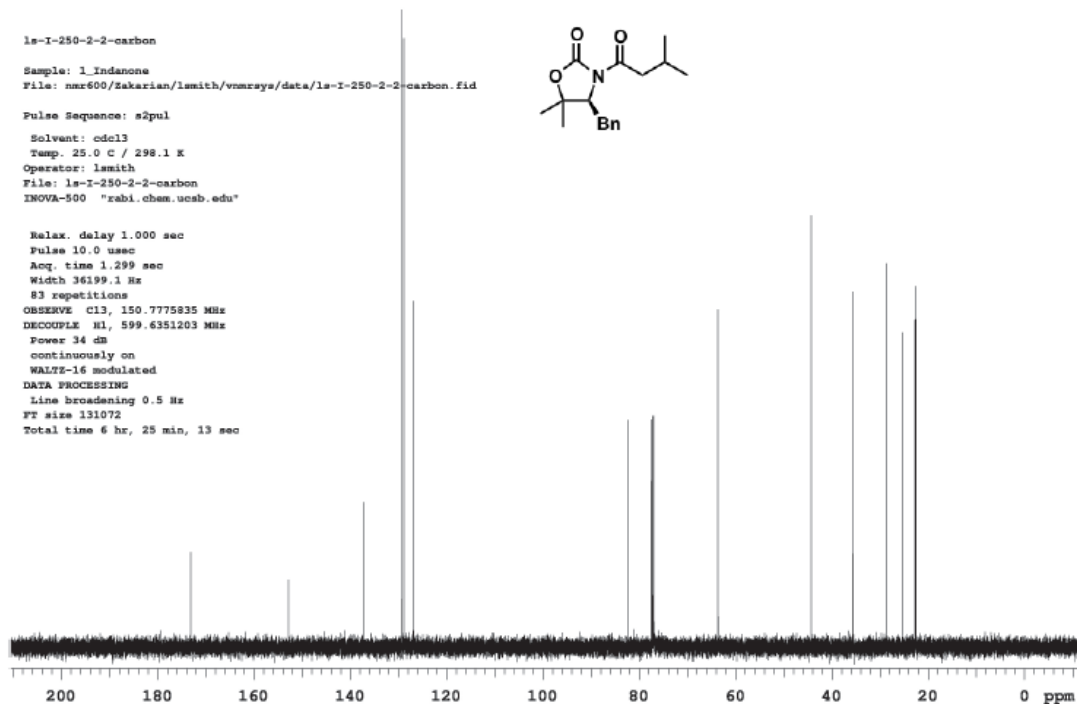
Operator: lsmith

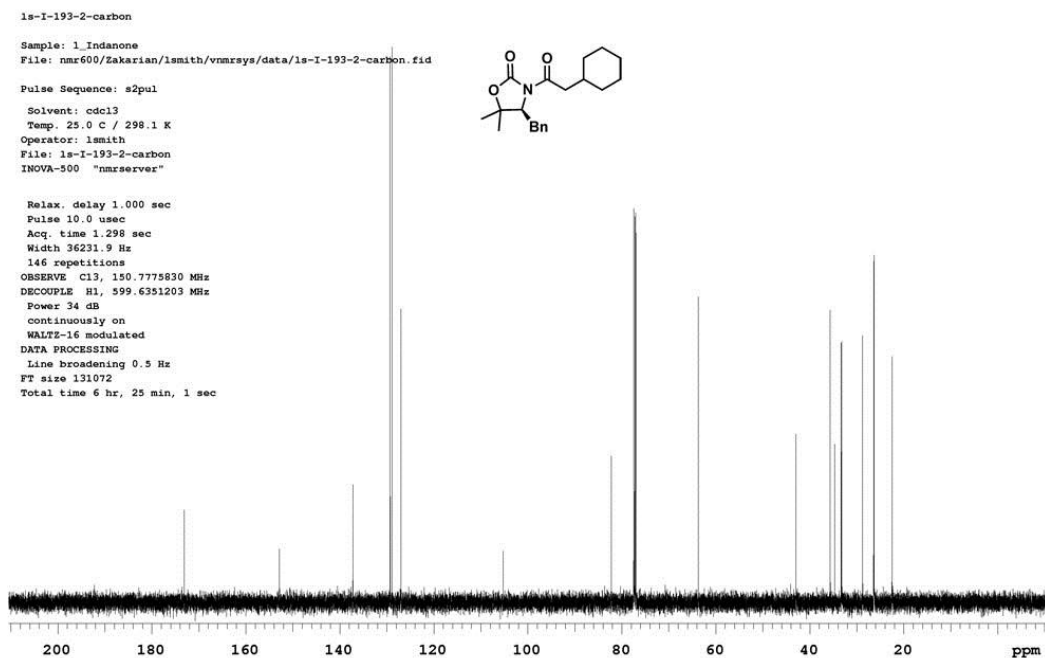
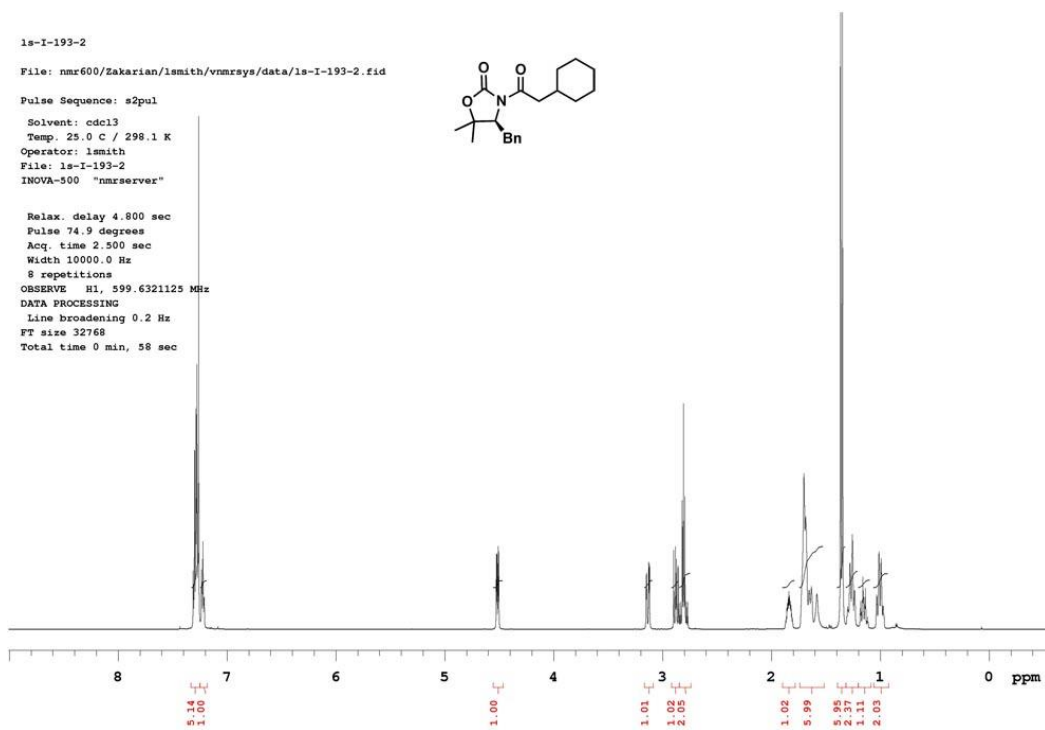
File: ls-I-250-2-2-carbon

INOVA-500 "xabi.chem.ucsb.edu"



Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
83 repetitions
OBSERVE C13, 150.7775835 MHz
DECOUPLE H1, 599.6351203 MHz
Powers 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec





ls-I-277-2

File: nmr600/Zakarian/lsmith/vnmrsvs/data/ls-I-277-2.fid

Pulse Sequence: s2pul

Solvent: cdcl3

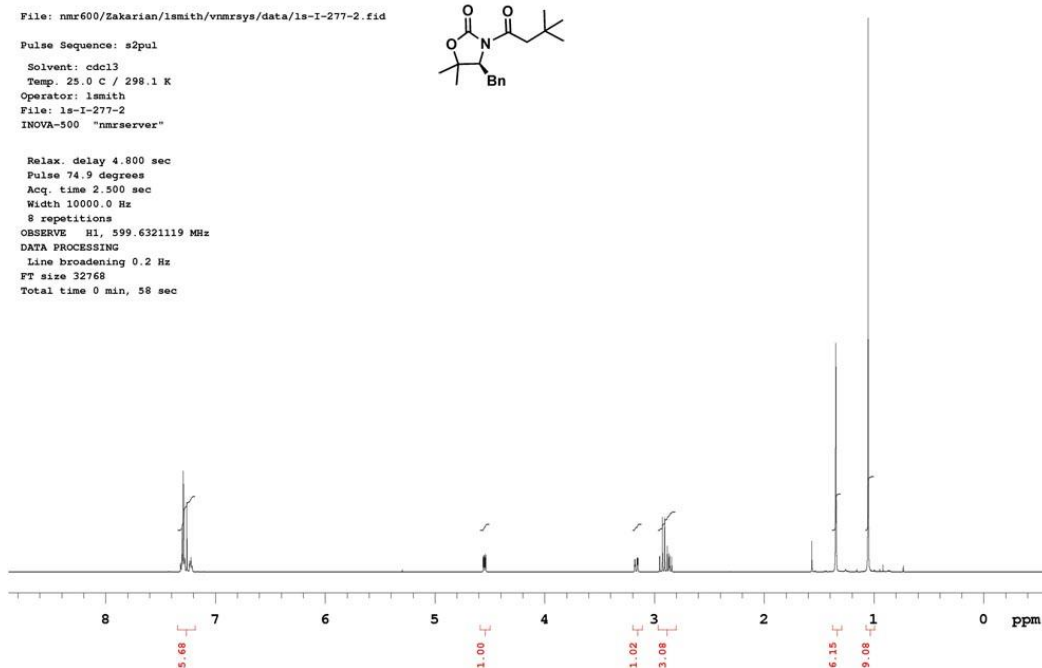
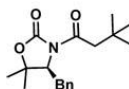
Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-277-2

INOVA-500 "nmrserver"

Relax. delay 4.800 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6321119 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 0 min, 58 sec



ls-I-277-2-carbon

Sample: 1_Indanone

File: nmr600/Zakarian/lsmith/vnmrsvs/data/ls-I-277-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

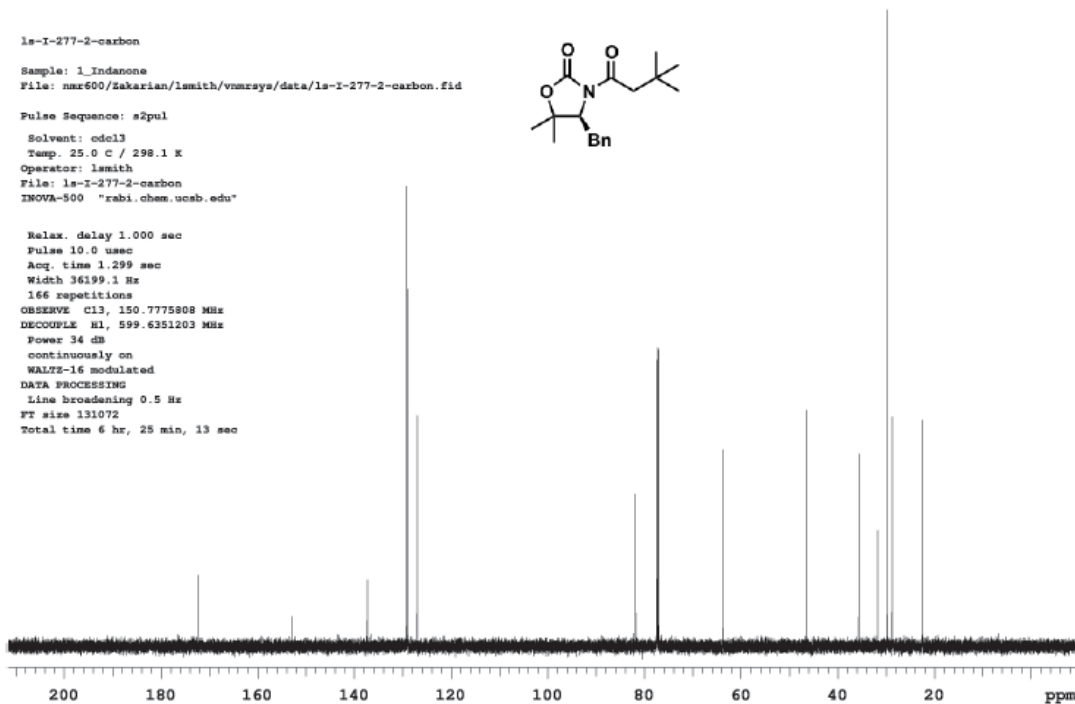
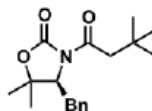
Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-277-2-carbon

INOVA-500 "rabi.chem.ucsb.edu"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
166 repetitions
OBSERVE C13, 150.7775908 MHz
DECOUPLE H1, 599.6351203 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec



ls-I-271-2

File: nmr600/Zakarian/lsmith/vnmrsvs/data/ls-I-271-2.fid

Pulse Sequence: s2pul

Solvent: cdcl3

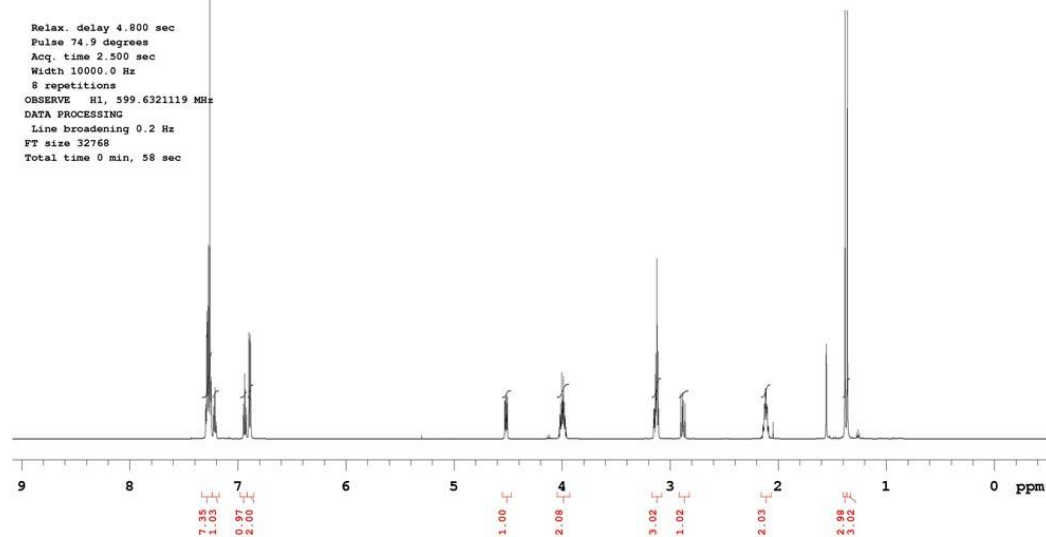
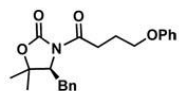
Temp: 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-271-2

INOVA-500 "nmrserver"

Relax. delay 4.800 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6321119 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 0 min, 58 sec



ls-I-271-2-carbon

Sample: 1_Indanone

File: nmr600/Zakarian/lsmith/vnmrsvs/data/ls-I-271-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

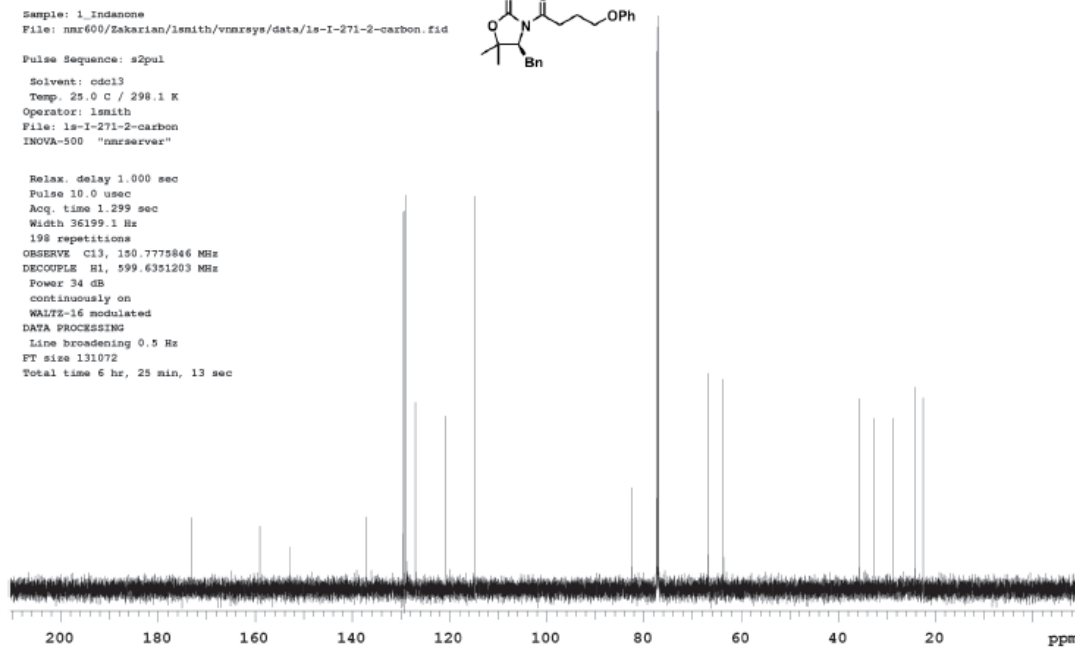
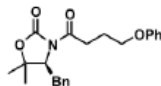
Temp: 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-271-2-carbon

INOVA-500 "nmrserver"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
198 repetitions
OBSERVE C13, 150.7775846 MHz
DECOUPLE H1, 599.6351203 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec



ls-I-cmpd9

File: nmr600/Zakarian/lsmith/vnmrsvs/data/ls-I-cmpd9.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-cmpd9

INOVA-500 "nmrserver"

Relax. delay 4.800 sec

Pulse 74.9 degrees

Acq. time 2.500 sec

Width 10000.0 Hz

8 repetitions

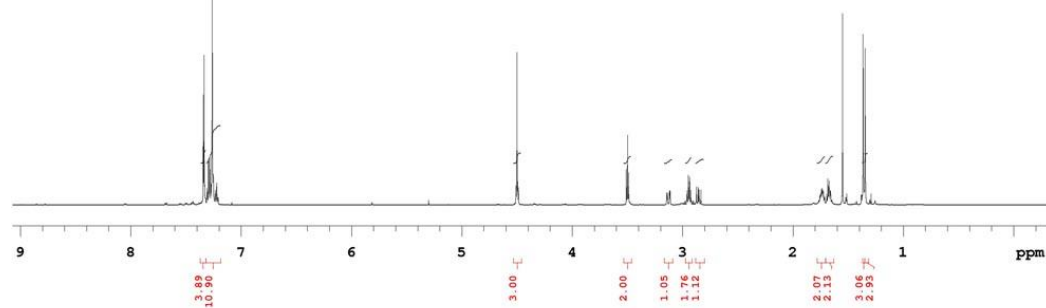
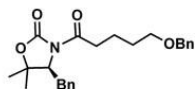
OBSERVE H1, 599.6321119 MHz

DATA PROCESSING

Line broadening 0.2 Hz

FT size 32768

Total time 0 min, 58 sec



ls-I-286-2-carbon

Sample: 1_Indanone

File: nmr600/Zakarian/lsmith/vnmrsvs/data/ls-I-286-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-286-2-carbon

INOVA-500 "rabi.chem.ucsb.edu"

Relax. delay 1.000 sec

Pulse 10.0 usec

Acq. time 1.299 sec

Width 36199.1 Hz

378 repetitions

OBSERVE C13, 150.7775828 MHz

DECOUPLE H1, 599.6351203 MHz

Power 34 dB

continuously on

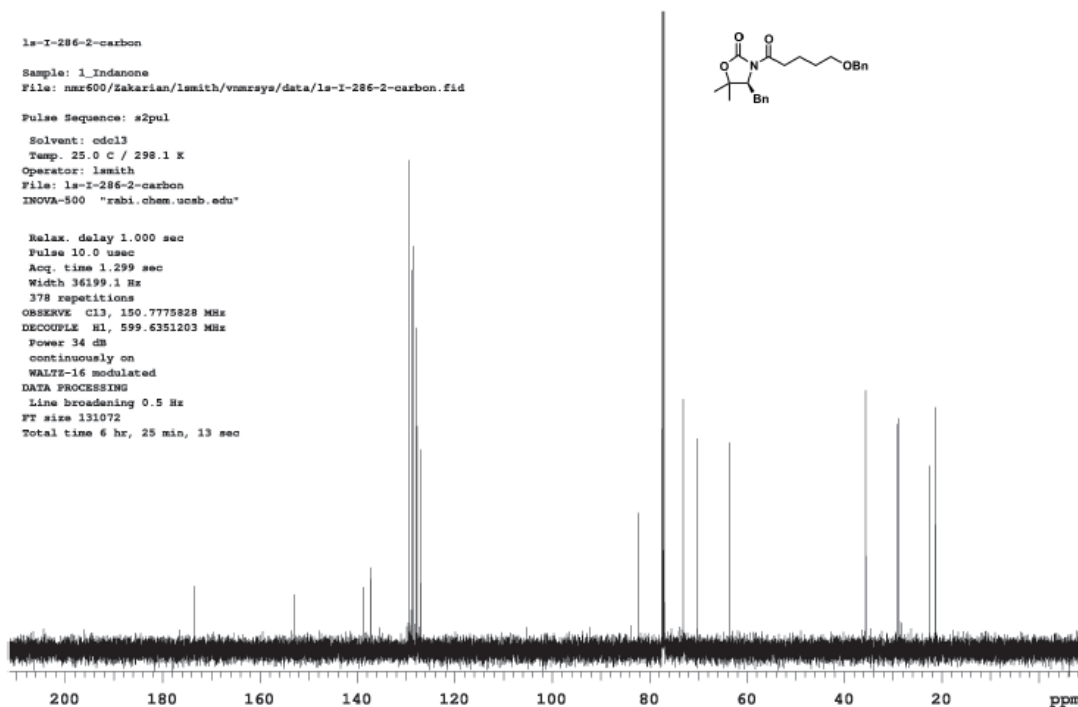
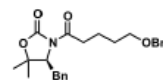
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 131072

Total time 6 hr, 25 min, 13 sec



ls-I-295-2

File: nmr600/Zakarian/lsmith/vnmrsys/data/ls-I-265-2.fid

Pulse Sequence: s2pul

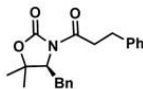
Solvent: cdcl3

Temp. 25.0 C / 298.1 K

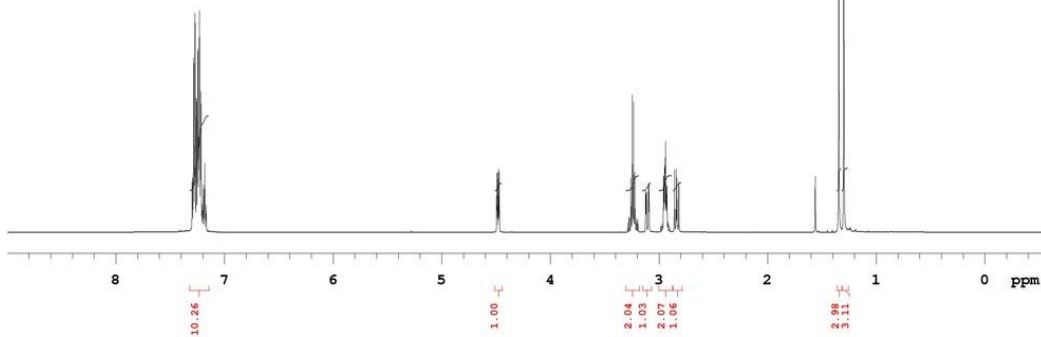
Operator: lsmith

File: ls-I-265-2

INOVA-500 "nmrserver"



Relax. delay 4.800 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6321234 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 0 min, 58 sec



ls-I-265-2-carbon

Sample: 1.Indanone

File: nmr600/Zakarian/lsmith/vnmrsys/data/ls-I-265-2-carbon.fid

Pulse Sequence: s2pul

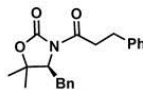
Solvent: cdcl3

Temp. 25.0 C / 298.1 K

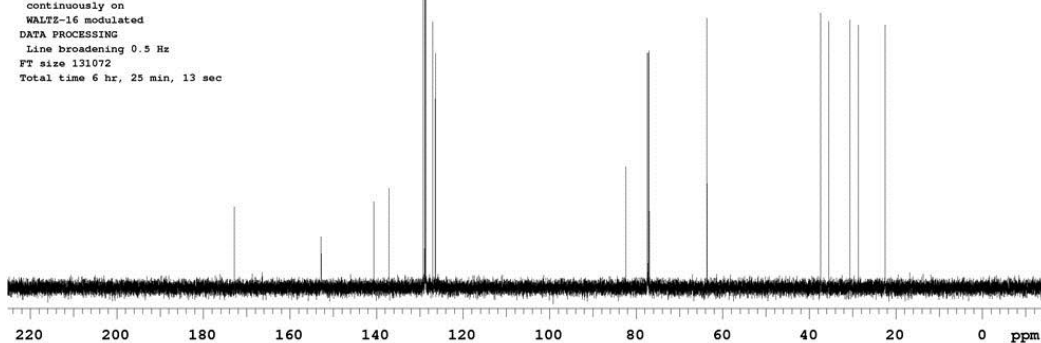
Operator: lsmith

File: ls-I-265-2-carbon

INOVA-500 "nmrserver"



Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
47 repetitions
OBSERVE C13, 150.7775901 MHz
DECOUPLE H1, 599.6351203 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec



ls-I-269-2

File: nmr600/Zakarian/lsmith/vmrsys/data/ls-I-269-2.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp: 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-269-2

INOVA-500 "nmrserver"

Relax. delay 4.800 sec

Pulse 74.9 degrees

Acq. time 2.500 sec

Width 10000.0 Hz

8 repetitions

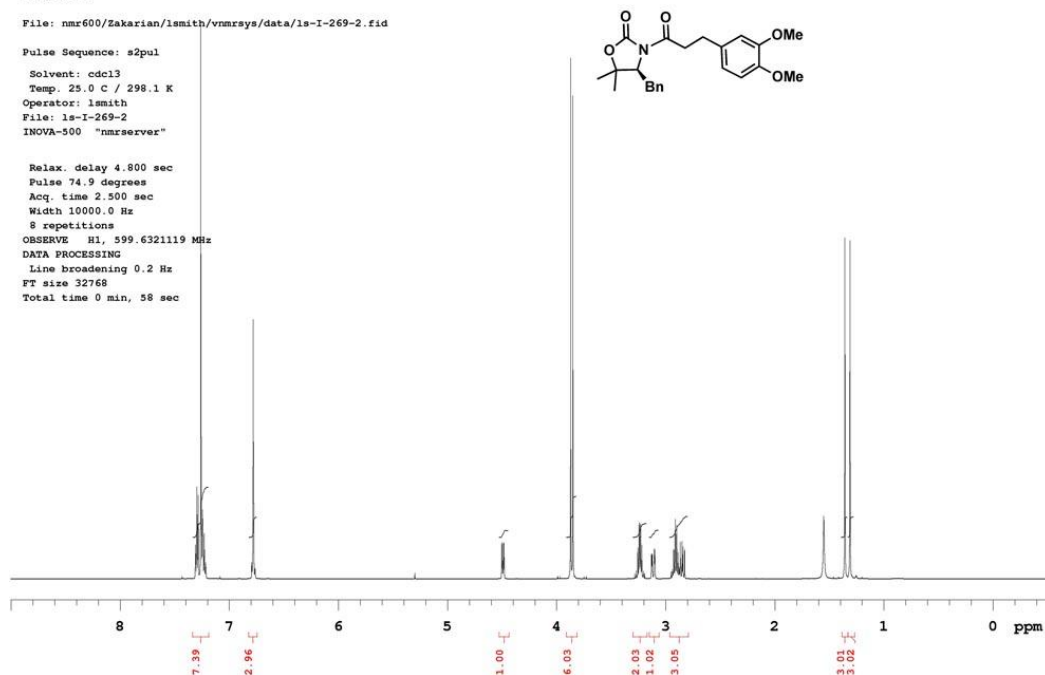
OBSERVE H1, 599.6321119 MHz

DATA PROCESSING

Line broadening 0.2 Hz

FT size 32768

Total time 0 min, 58 sec



ls-I-269-2-carbon

Sample: 1. Indanone

File: nmr600/Zakarian/lsmith/vmrsys/data/ls-I-269-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp: 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-269-2-carbon

INOVA-500 "nmrserver"

Relax. delay 1.000 sec

Pulse 10.0 usec

Acq. time 1.299 sec

Width 36199.1 Hz

412 repetitions

OBSERVE C13, 150.7775817 MHz

DECOUPLE H1, 599.6351203 MHz

Power 34 dB

continuously on

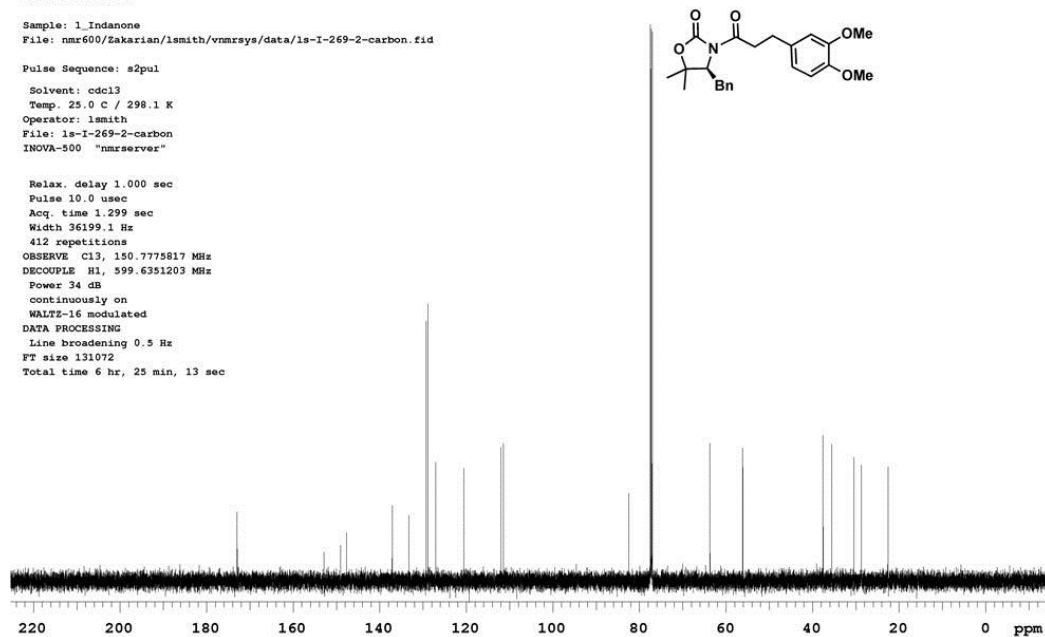
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 131072

Total time 6 hr, 25 min, 13 sec



ls-I-188-2-2

File: nmr600/Zakarian/lsmith/vmrsys/data/ls-I-188-2-2.fid

Pulse Sequence: s2pul

Solvent: cdcl3

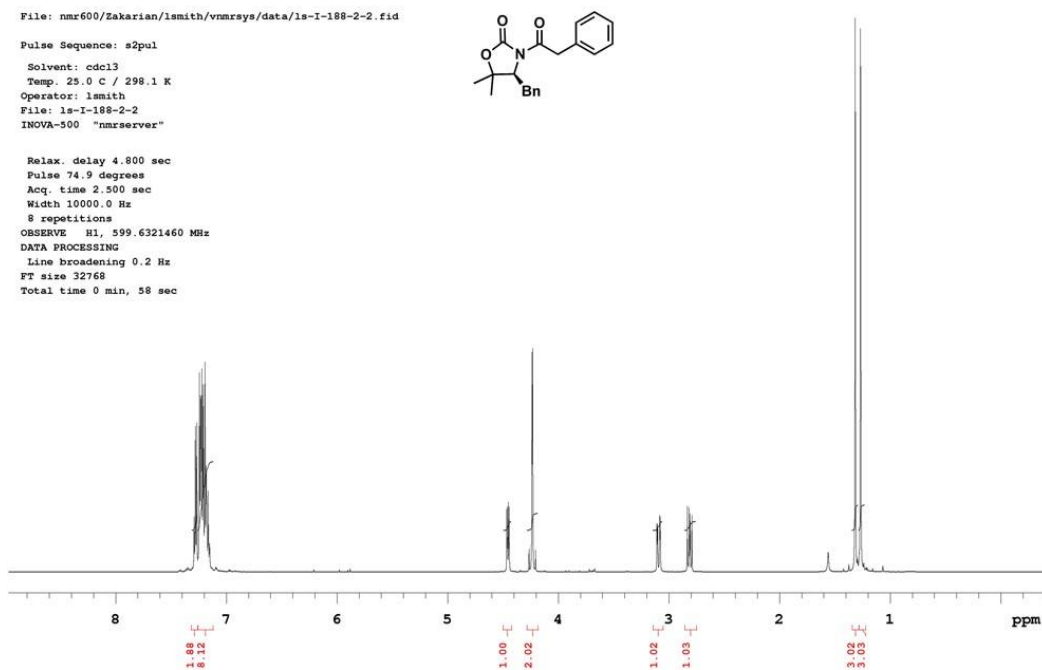
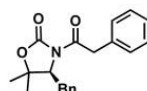
Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-188-2-2

INOVA-500 "nmrserver"

Relax. delay 4.800 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6321460 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 0 min, 58 sec



ls-I-188-2-carbon

Sample: 1. Indanone

File: nmr600/Zakarian/lsmith/vmrsys/data/ls-I-188-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

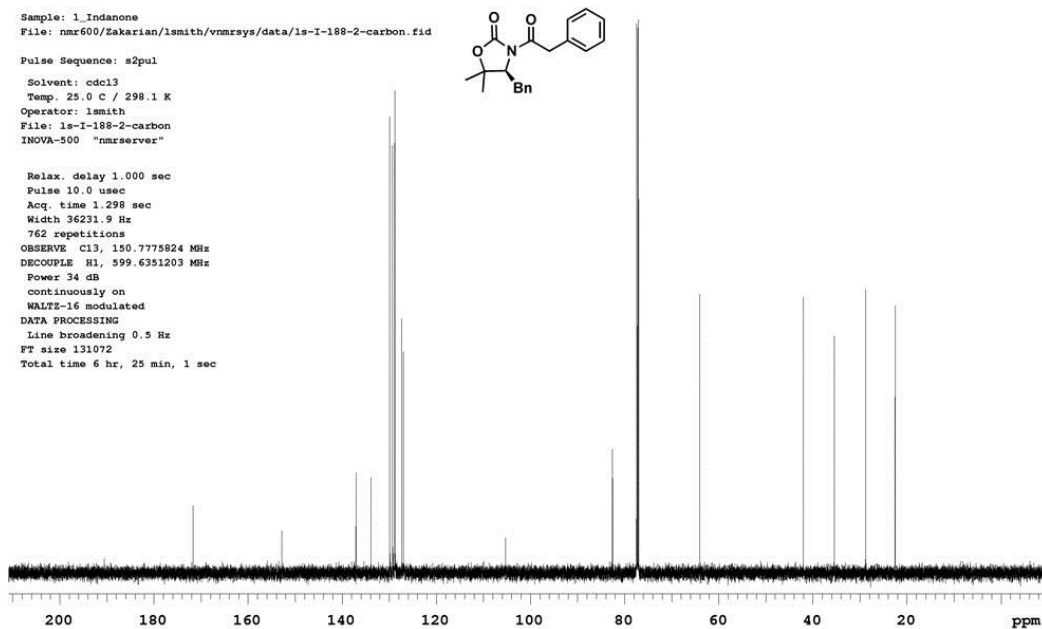
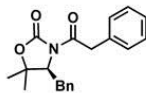
Temp. 25.0 C / 298.1 K

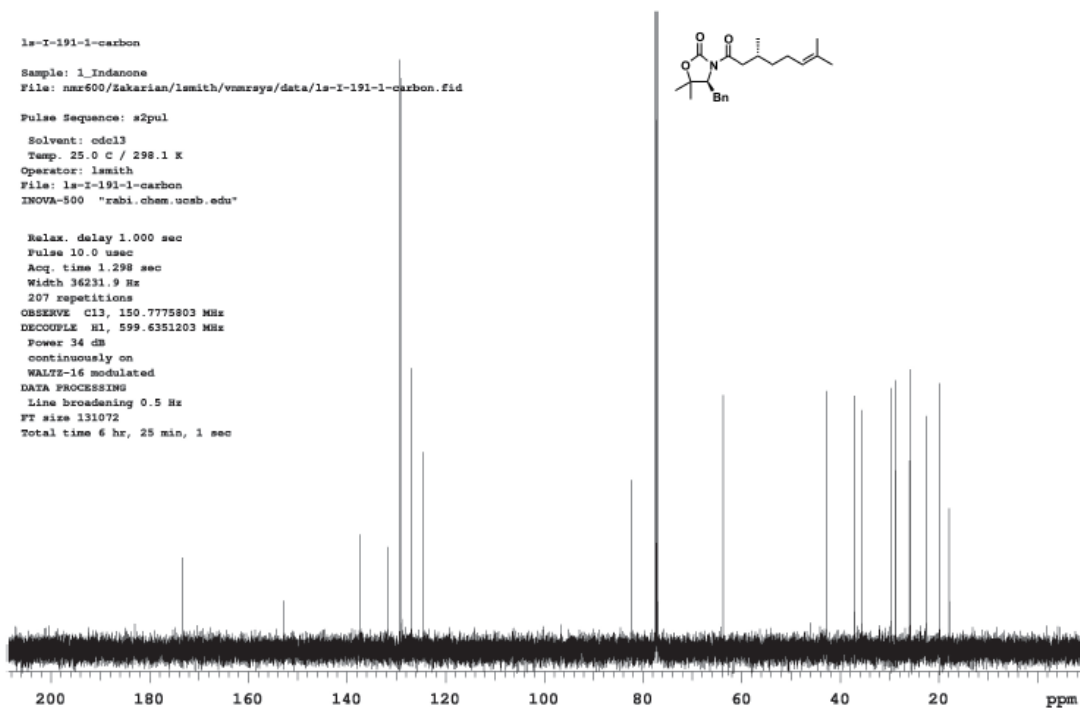
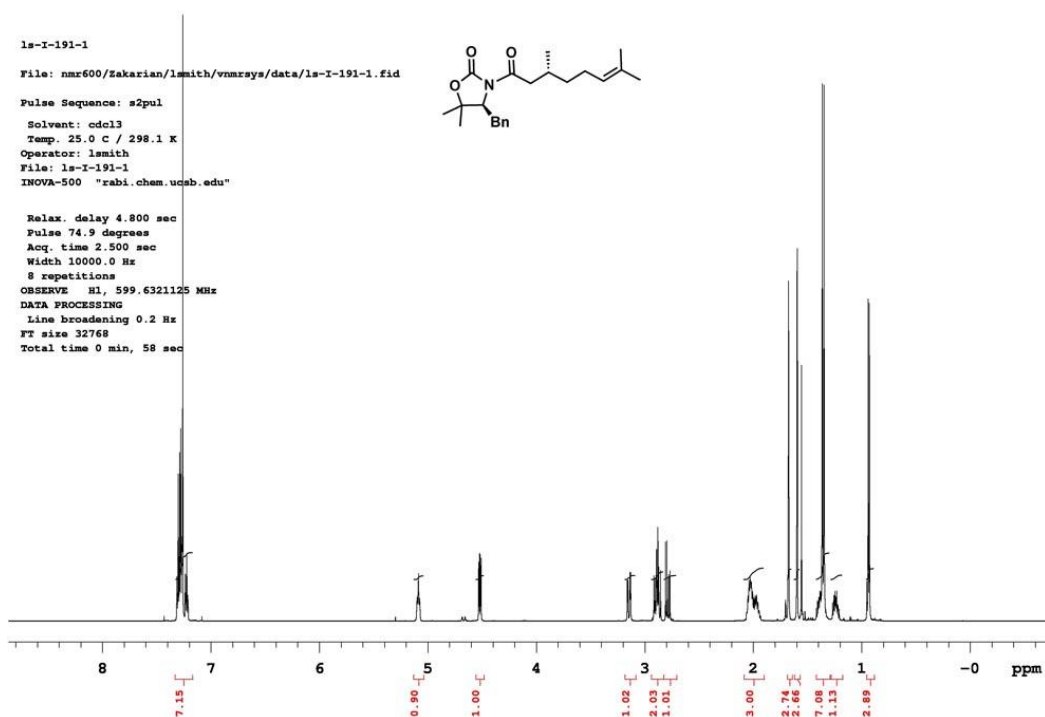
Operator: lsmith

File: ls-I-188-2-carbon

INOVA-500 "nmrserver"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.298 sec
Width 36231.9 Hz
762 repetitions
OBSERVE C13, 150.7775824 MHz
DECOUPLE H1, 599.6351203 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 1 sec





ls-I-273-2-2

File: nmr600/Zakarian/lsmith/vmrsys/data/ls-I-273-2-2.fid

Pulse Sequence: s2pul

Solvent: cdcl3

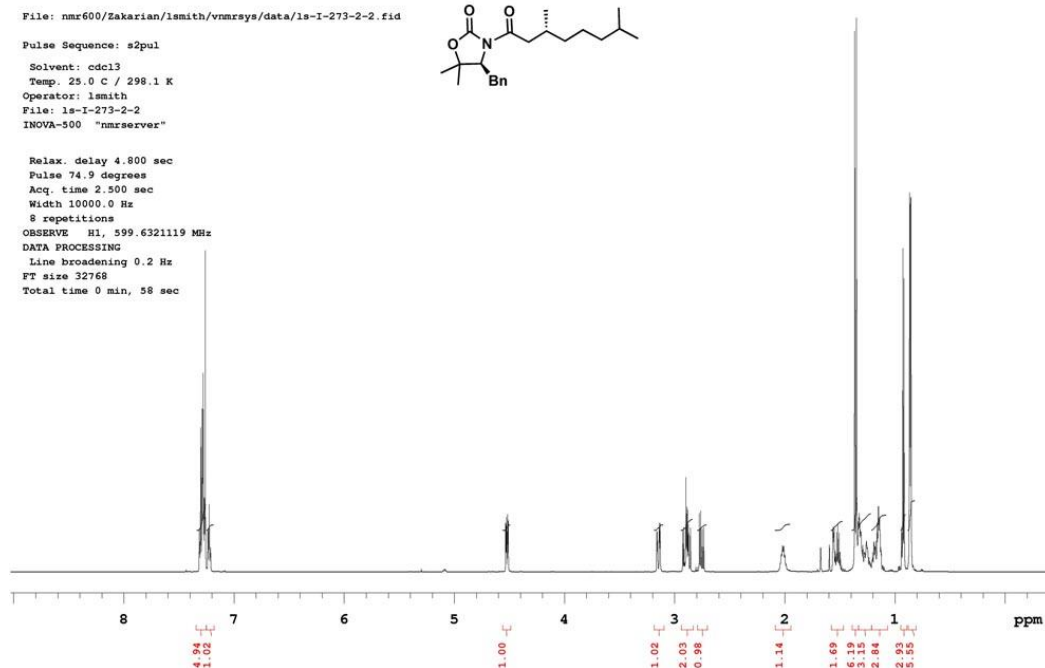
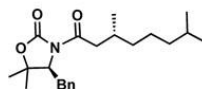
Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-I-273-2-2

INOVA-500 "nmrserver"

Relax. delay 4.800 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6321119 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 0 min, 58 sec



ls-I-273-2-2-carbon

Sample: 1. Indanone
File: nmr600/Zakarian/lsmith/vmrsys/data/ls-I-273-2-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

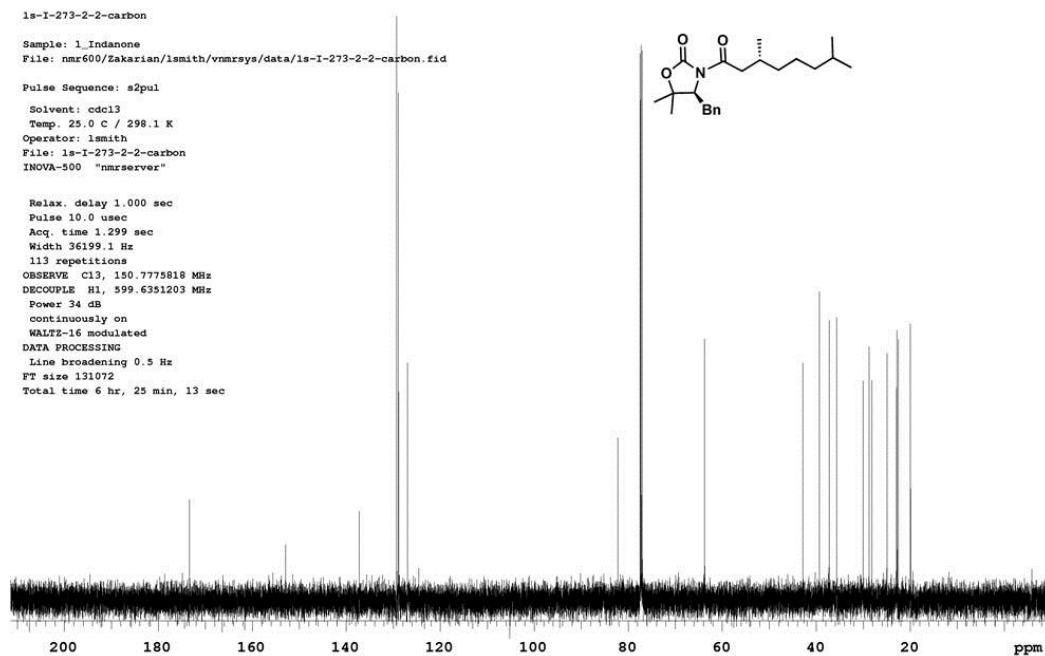
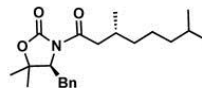
Temp. 25.0 C / 298.1 K

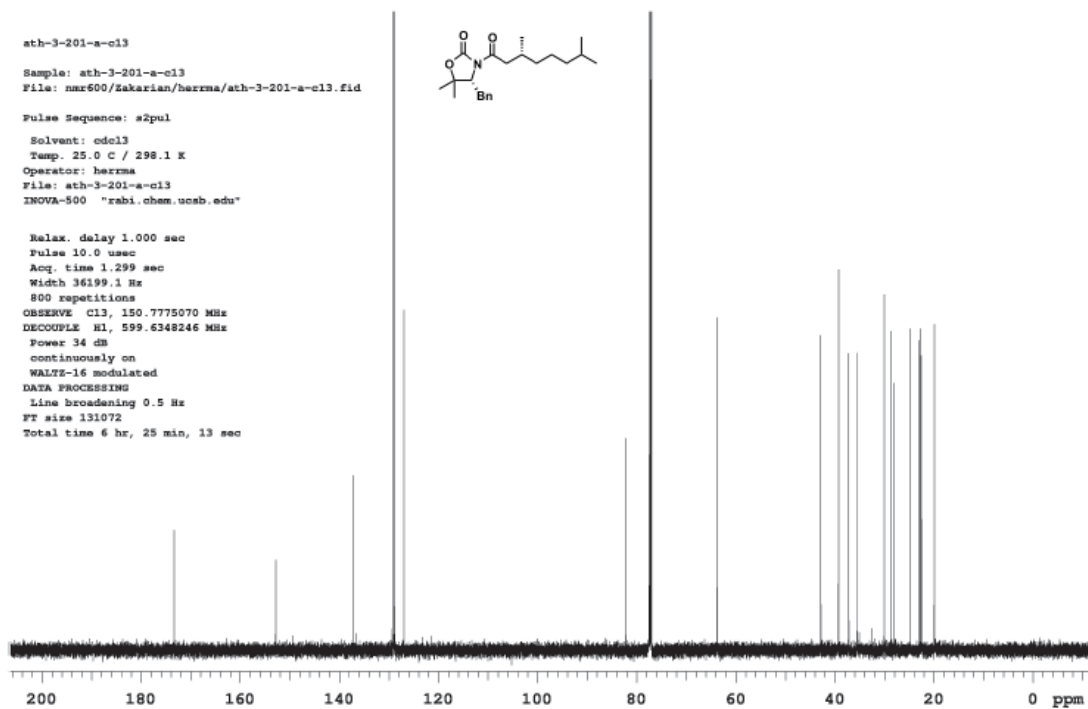
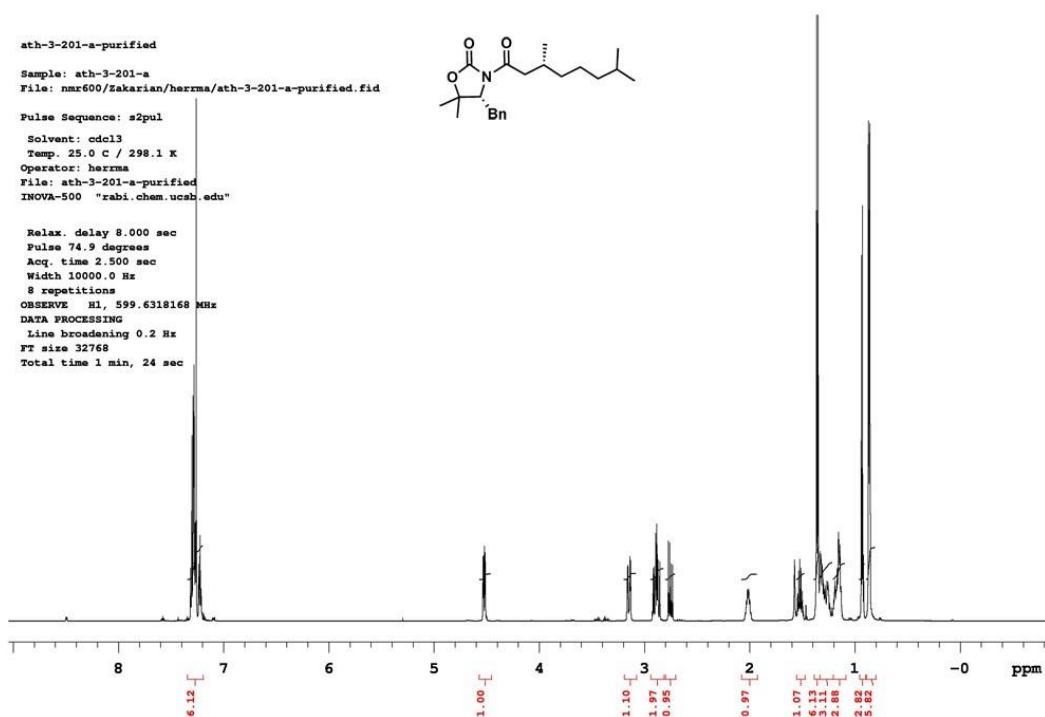
Operator: lsmith

File: ls-I-273-2-2-carbon

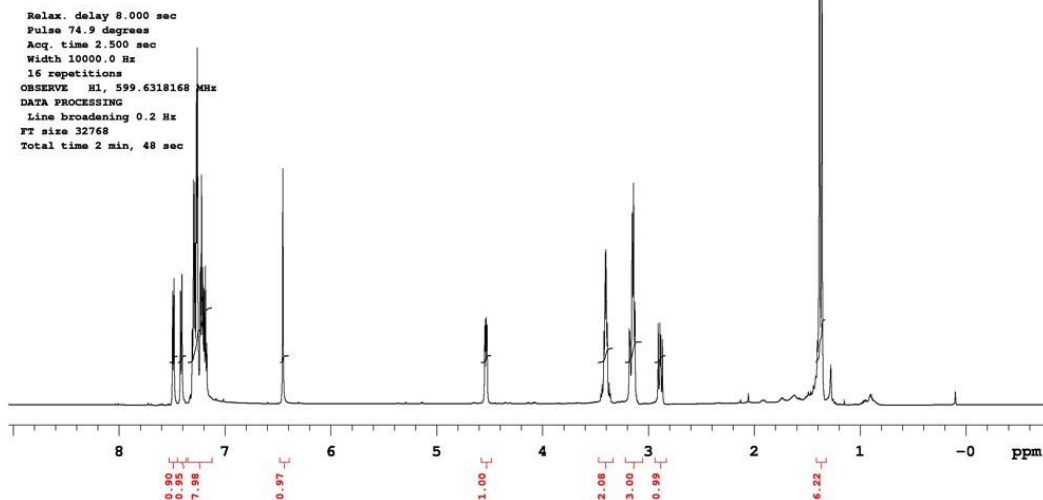
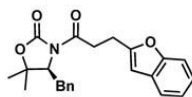
INOVA-500 "nmrserver"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
113 repetitions
OBSERVE C13, 150.7775818 MHz
DECOUPLE H1, 599.6351203 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec

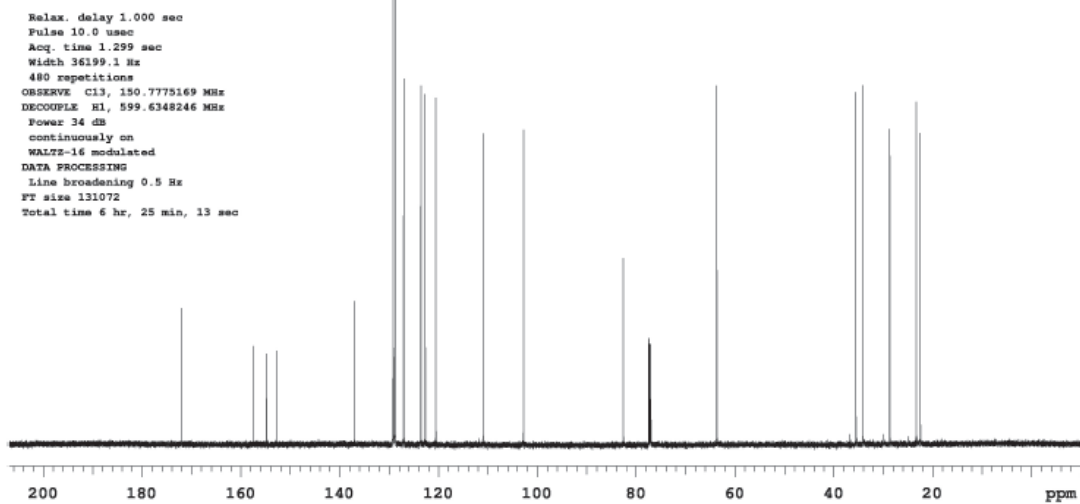
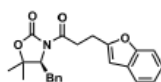


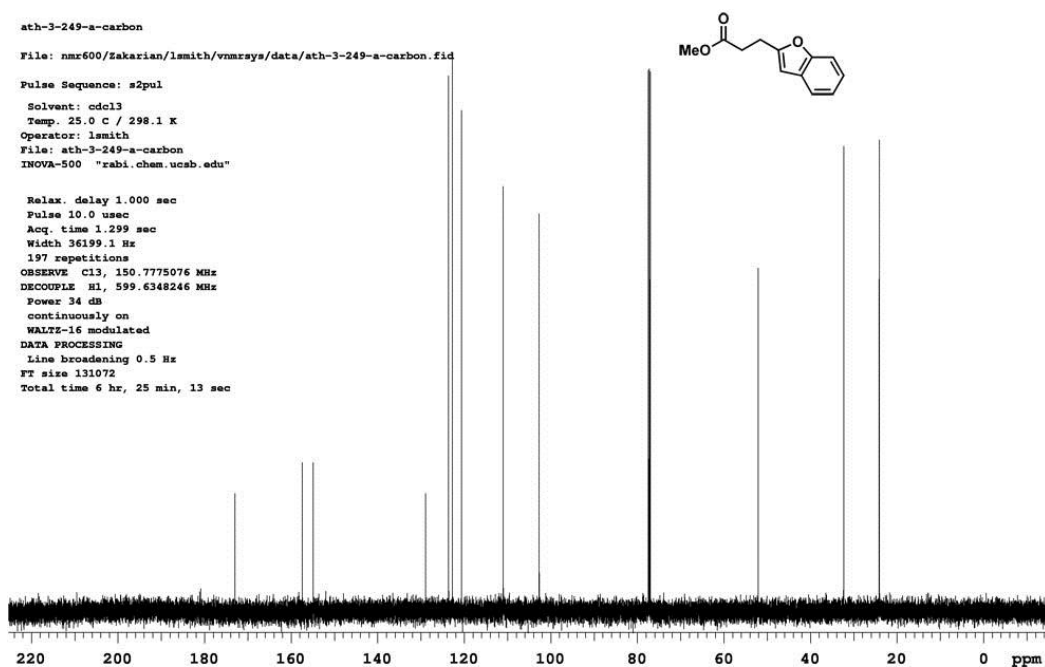
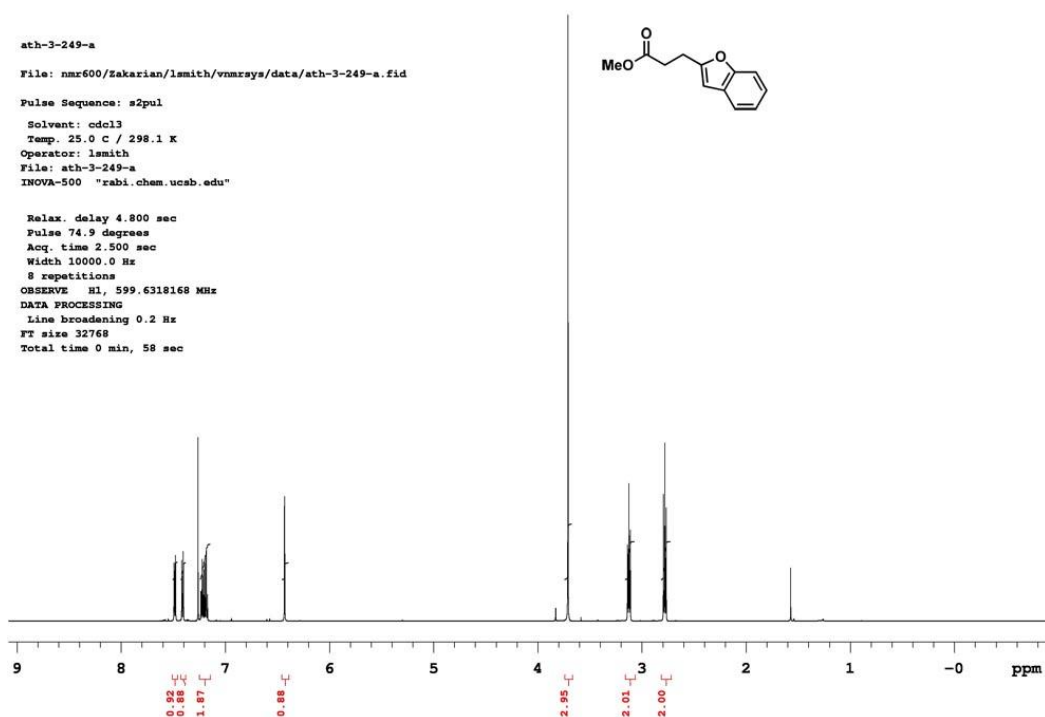


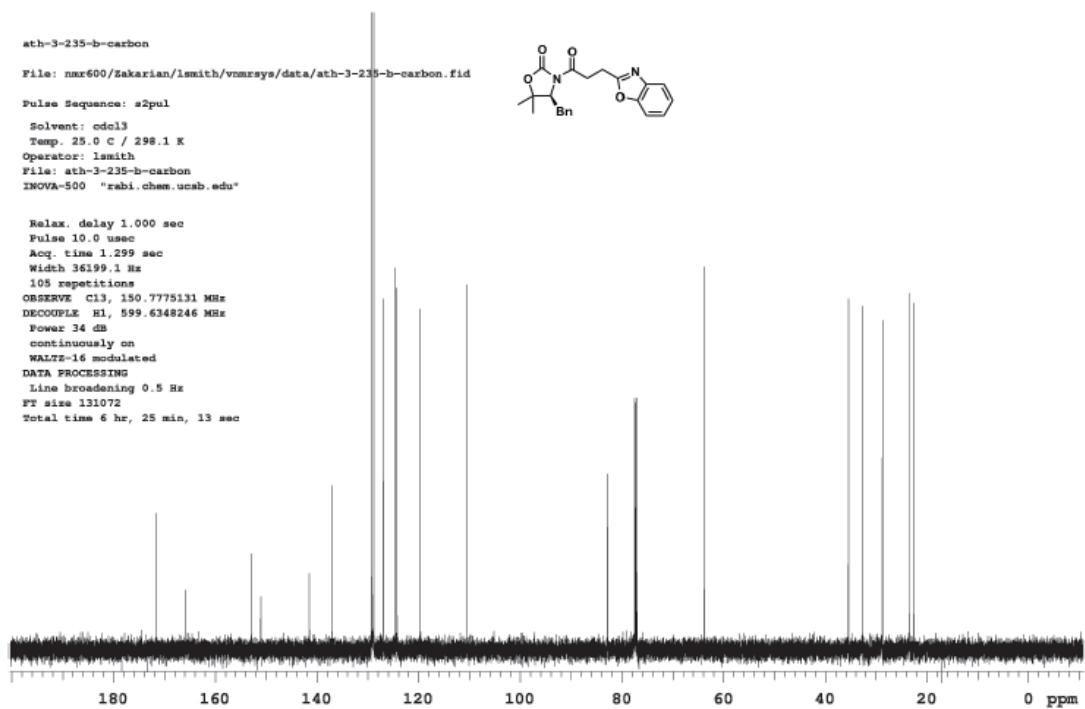
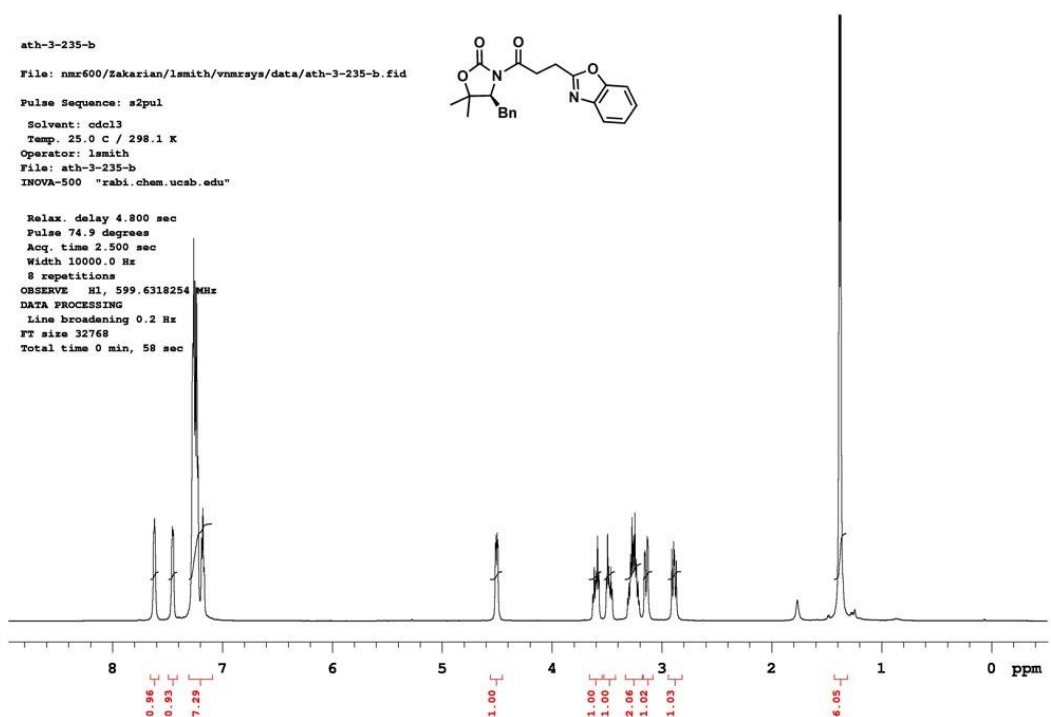
ath-3-252-a-AB
 Sample: ath-3-252-b-AB
 File: nmr600/Zakarian/herma/ath-3-252-a-AB.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp. 25.0 C / 298.1 K
 Operator: herma
 File: ath-3-252-a-AB
 INOVA-500 "rabi.chem.ucsb.edu"



ath-3-252-b-AB-c13
 File: nmr600/Zakarian/herma/ath-3-252-b-AB-c13.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp. 25.0 C / 298.1 K
 Operator: herma
 File: ath-3-252-b-AB-c13
 INOVA-500 "rabi.chem.ucsb.edu"





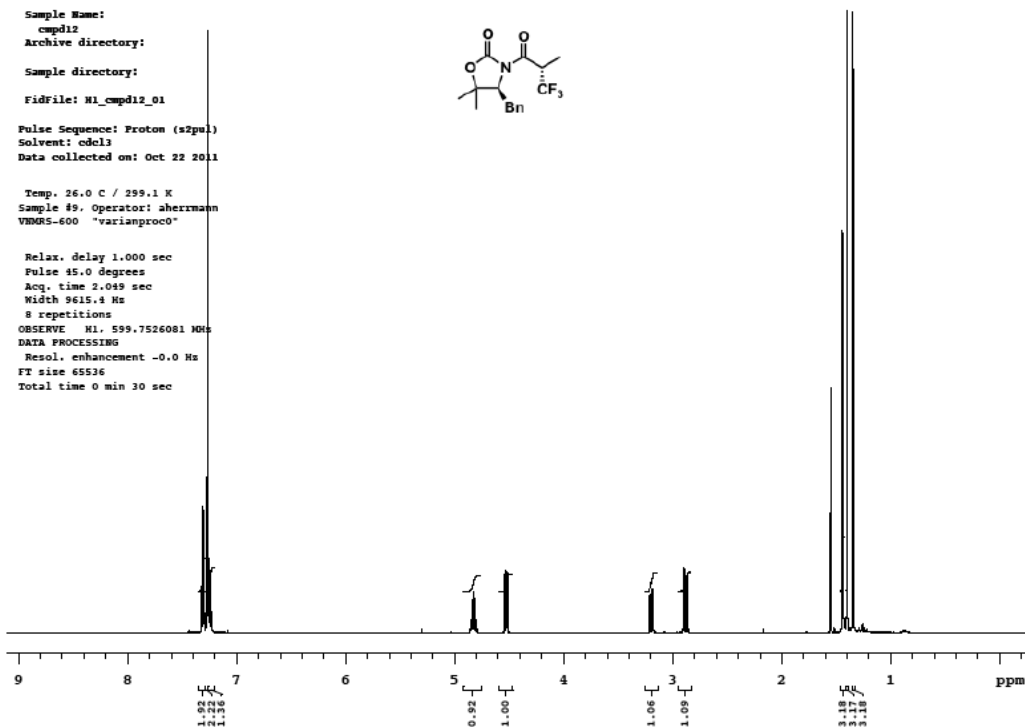
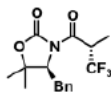


ath-3-176-a
600 MHz

Sample Name:
cmpd12
Archive directory:
Sample directory:
FidFile: M1_cmpd12_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011

Temp. 26.0 C / 299.1 K
Sample #9. Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE M1. 599.7526081 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec

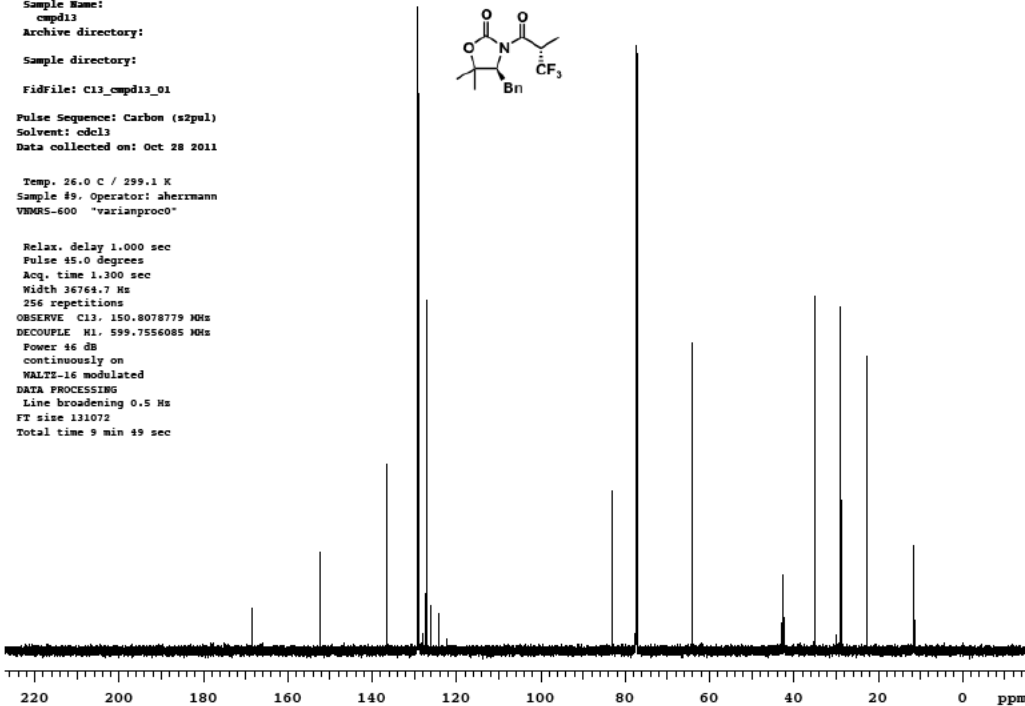
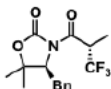


13C

Sample Name:
cmpd13
Archive directory:
Sample directory:
FidFile: C13_cmpd13_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011

Temp. 26.0 C / 299.1 K
Sample #9. Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
256 repetitions
OBSERVE C13. 150.8078779 MHz
DECOUPLE M1. 599.7556085 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min 49 sec



19F
ath-3-176-a
600 MHz

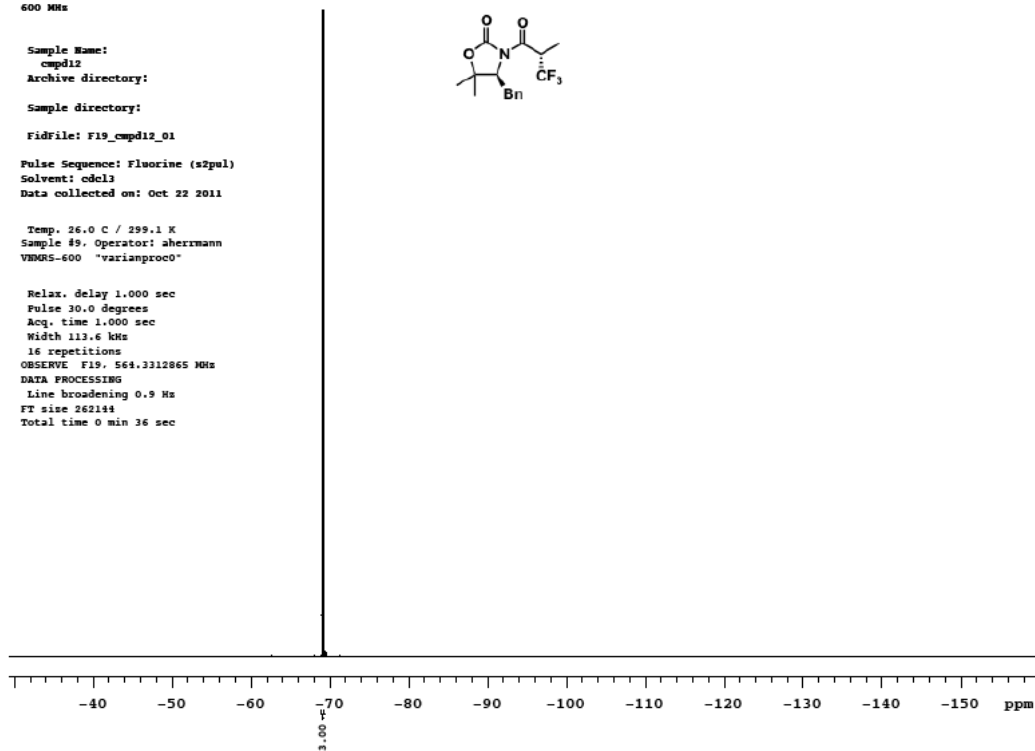
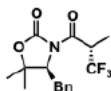
Sample Name:
compd12
Archive directory:
Sample directory:

Fidfile: F19_compd12_01

Pulse Sequence: Fluorine (s2ps1)
Solvent: cdcl3
Data collected on: Oct 22 2011

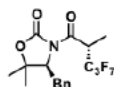
Temp. 26.0 C / 299.1 K
Sample #9, Operator: aherrmann
VND65-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec

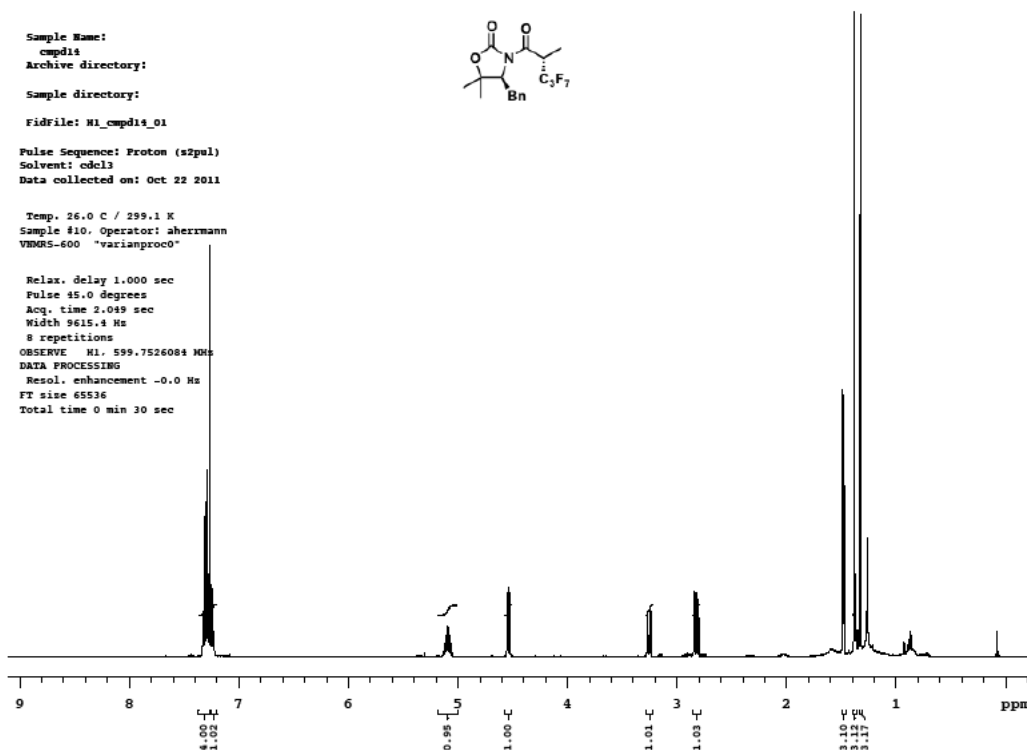


1H
600 MHz

Sample Name:
cmpd14
Archive directory:
Sample directory:
FidFile: M1_cmpd14_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011



Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VPMAS-600 "varianproc0"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE M1, 599.7526084 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec

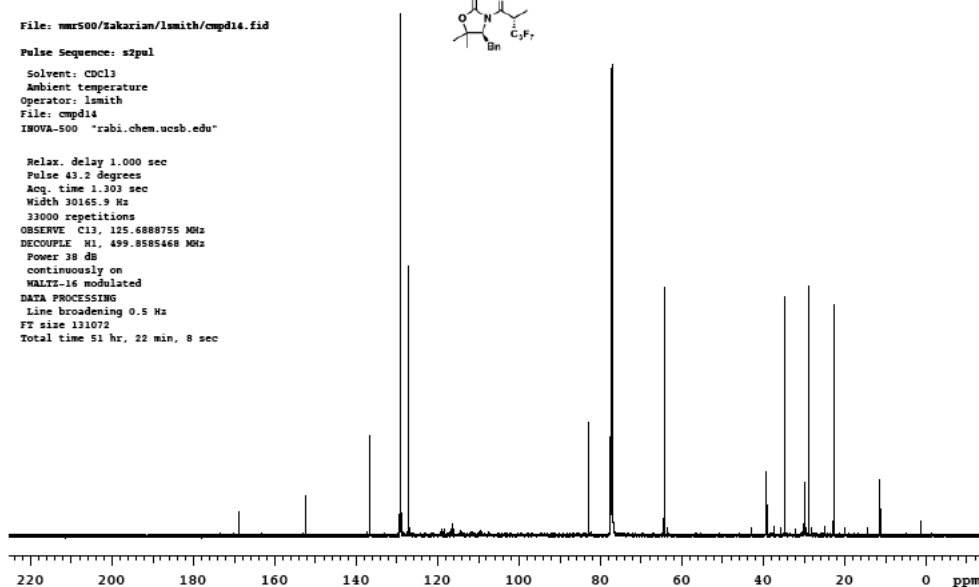


Std carbon

File: mmr500/Yakarian/lsmith/cmpd14.fid
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Operator: lsmith
File: cmpd14
INOVA-500 "rabi.chem.ucsb.edu"



Relax. delay 1.000 sec
Pulse 43.2 degrees
Acq. time 1.303 sec
Width 30165.9 Hz
31000 repetitions
OBSERVE C13, 125.6889755 MHz
DECOUPLE M1, 499.8585468 MHz
Power 38 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 51 hr, 22 min, 8 sec

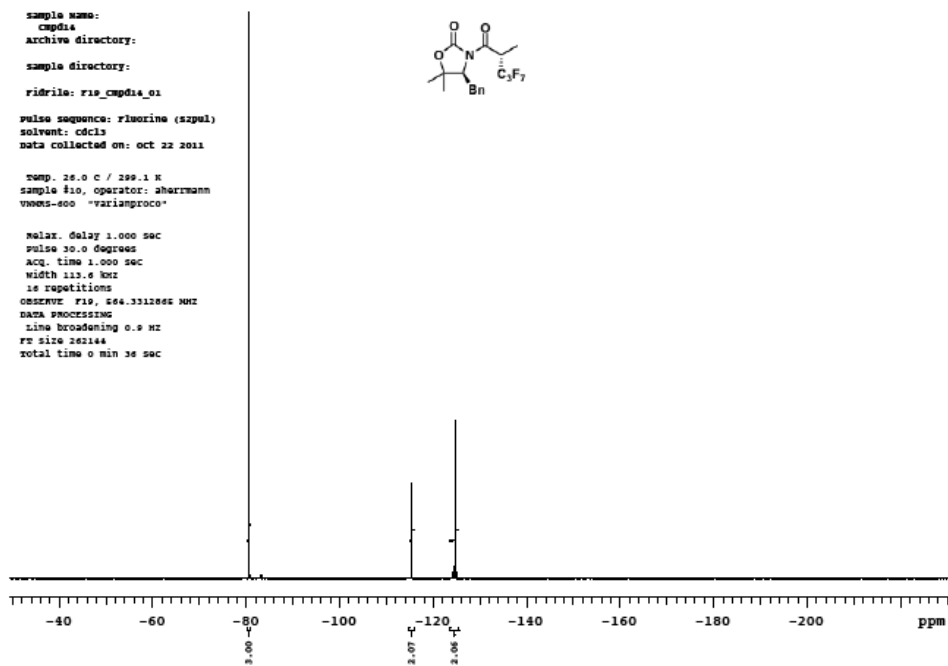
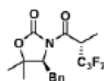


107
600 MHz

sample name:
cmpd14
archive directory:
sample directory:
fidfile: f14_cmpd14_01
pulse sequence: rbcprine (szpul)
solvent: cdcl3
data collected on: oct 22 2011

temp. 25.0 c / 299.1 k
sample #10, operator: aharrmann
vnmrs-600 "varianproce"

relax. delay 1.000 sec
pulse 10.0 degrees
acq. time 1.000 sec
width 113.6 kmz
16 repetitions
OBSERVE F10, 254.331266 MHz
DATA PROCESSING
line broadening 0.9 Hz
FT size 262144
total time 0 min 36 sec

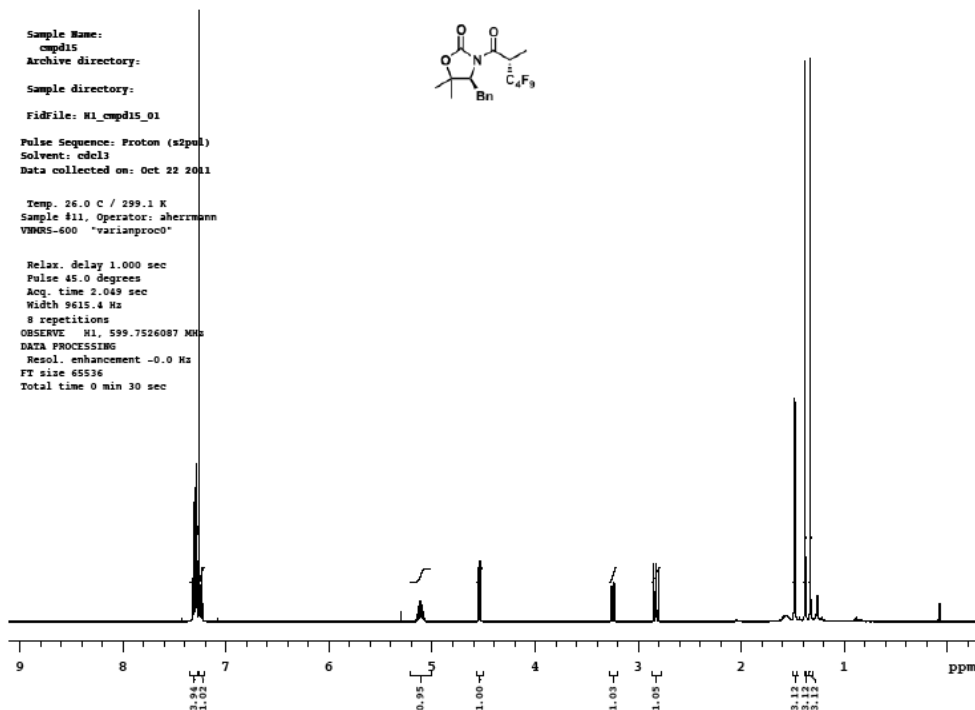
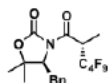


¹H
600 MHz

Sample Name: cmpd15
Archive directory:
Sample directory:
FidFile: H1_cmpd15_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011

Temp. 26.0 C / 299.1 K
Sample #11, Operator: aherrmann
VNMRS-600 "varianproco"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE H1, 599.7526087 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec

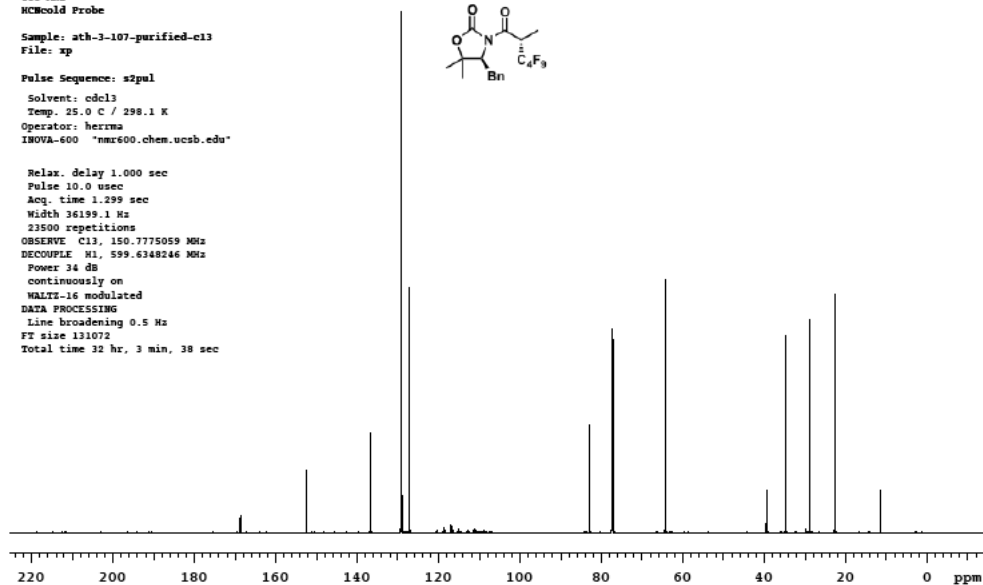
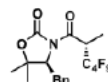


Date of experiment: Jan 2 2012
ath-3-107-purified-cl3
600 MHz
HCMWold Probe

Sample: ath-3-107-purified-cl3
File: xp

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: herma
INOVA-600 "nmr600.chem.ucsb.edu"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
23500 repetitions
OBSERVE C13, 150.7775059 MHz
DECOUPLE H1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 32 hr, 3 min, 38 sec

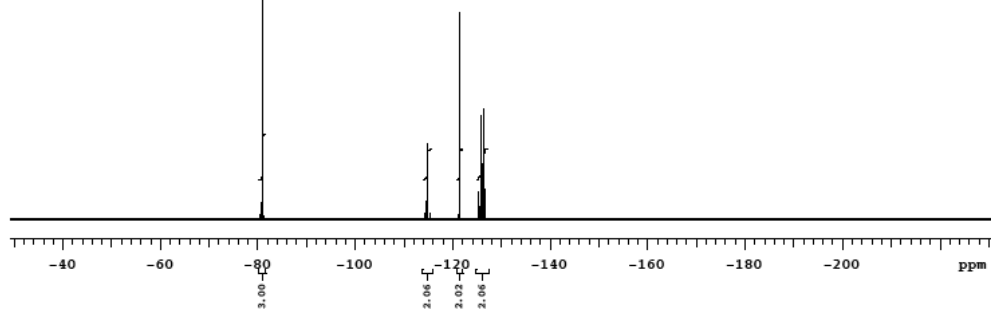
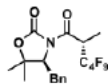


19F
600 MHz

Sample Name:
compd15
Archive directory:
Sample directory:
Fidfile: F19_compd15_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011

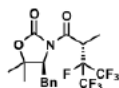
Temp. 26.0 C / 299.1 K
Sample #11, Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



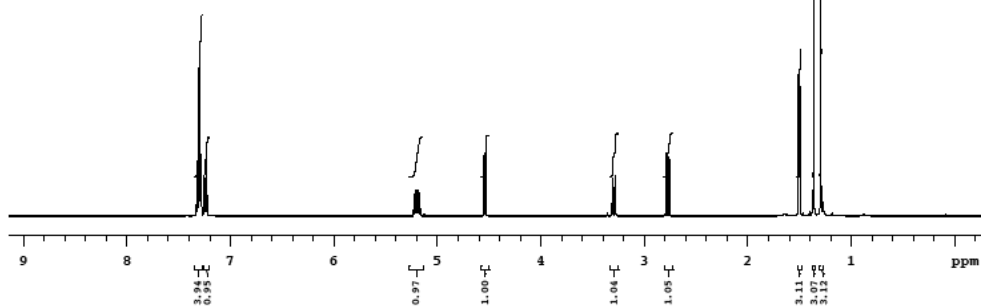
1H

Sample Name: cmpd16
Archive directory:
Sample directory:
FidFile: M1_cmpd16_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011



Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE M1, 599.7526075 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec

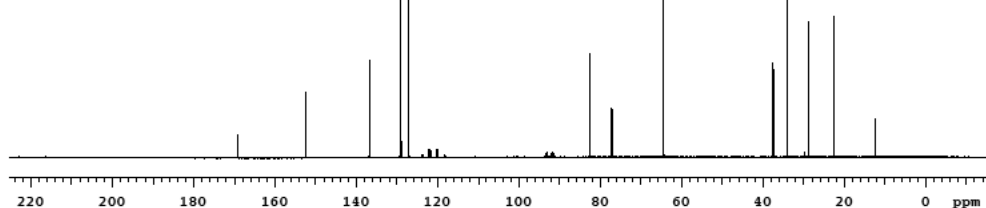


Std carbon

File: mmr600/Zakarian/lsmith/vnmrsys/data/1s-2-cmpd16-carbon.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: lsmith
File: 1s-2-cmpd16-carbon
INOVA-500 "rabi.chem.ucsb.edu"



Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
2301 repetitions
OBSERVE C13, 150.7775098 MHz
DECOUPLE M1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec

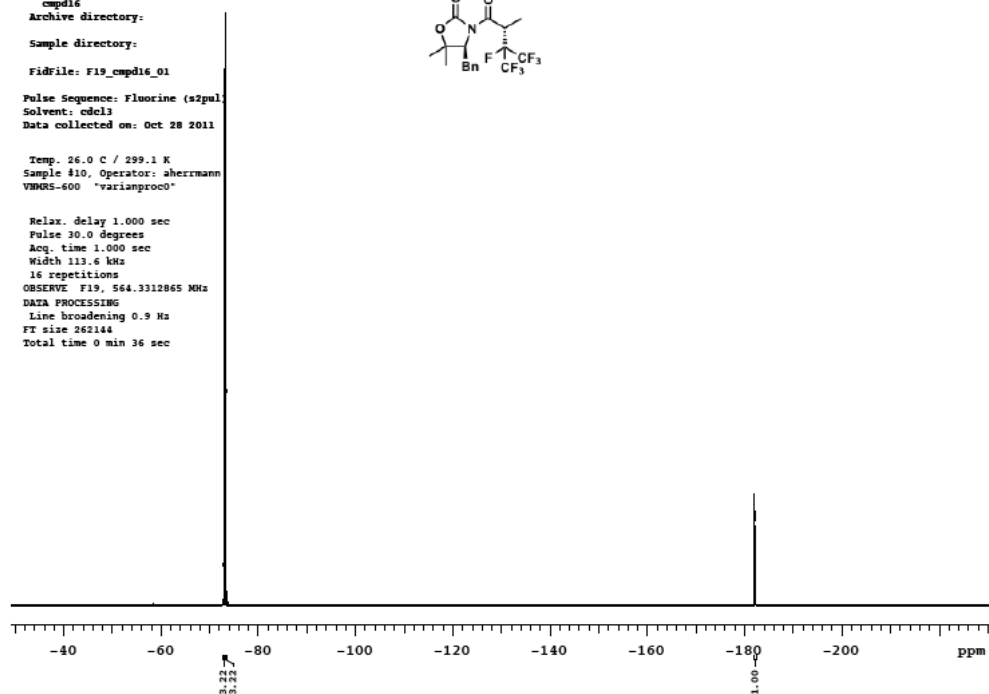
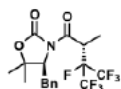


19F

Sample Name:
 compd16
Archive directory:
Sample directory:
Fidfile: F19_comp16_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011

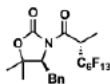
Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 16 sec



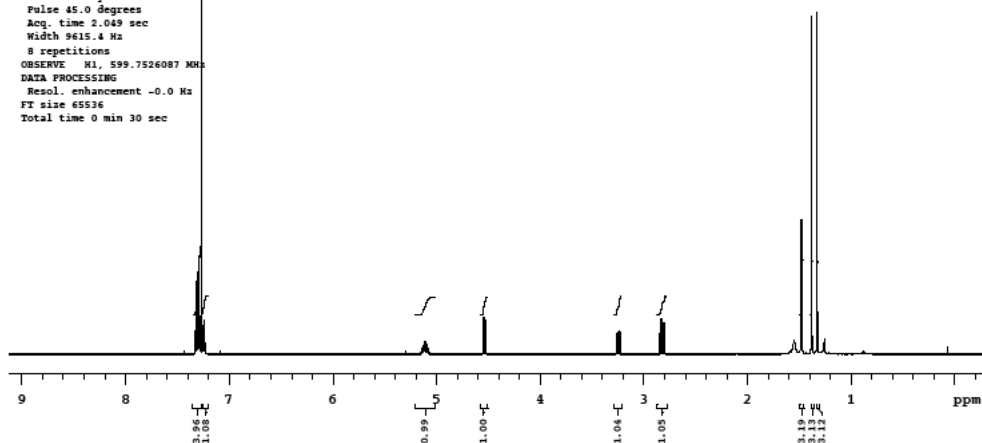
1H
600 MHz

Sample Name:
cmpd18
Archive directory:
Sample directory:
Fidfile: M1_cmpd18_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011

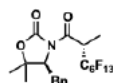


Temp. 26.0 C / 299.1 K
Sample #12, Operator: aherrmann
VNMRS-600 "varianproco"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE M1, 599.7526087 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec

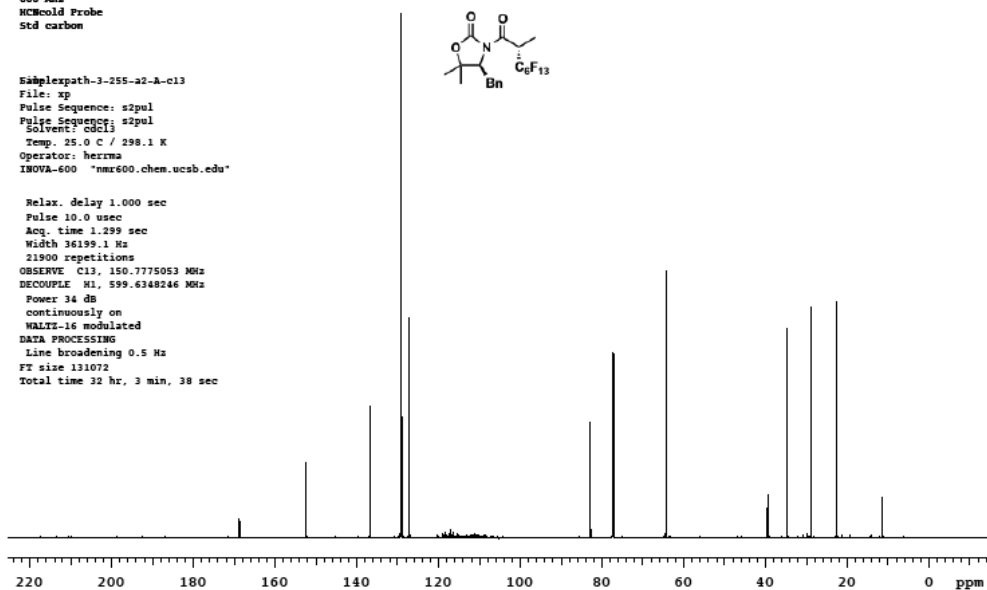


Date of experiment: Jan 3 2012
ath-3-255-a2-a-c13
600 MHz
HCRcold Probe
Std carbon



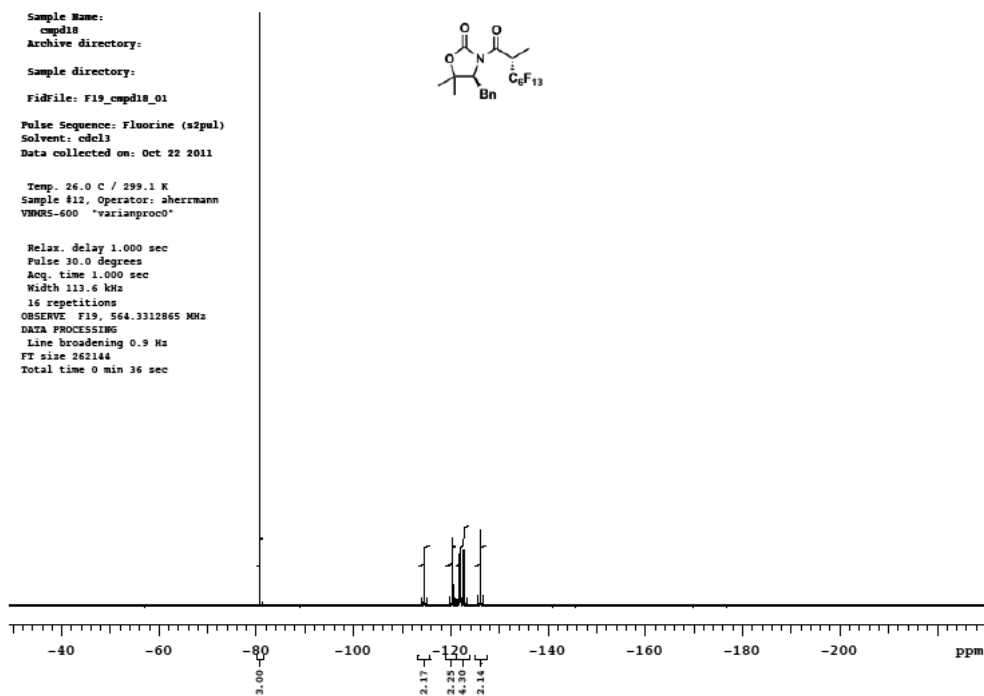
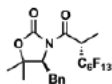
Samplepath-3-255-a2-a-c13
File: xp
Pulse Sequence: s2pul
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: herma
INOVA-600 "nmr600.chem.ucsb.edu"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
21900 repetitions
OBSERVE C13, 150.7775053 MHz
DECOUPLE M1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 32 hr, 3 min, 38 sec



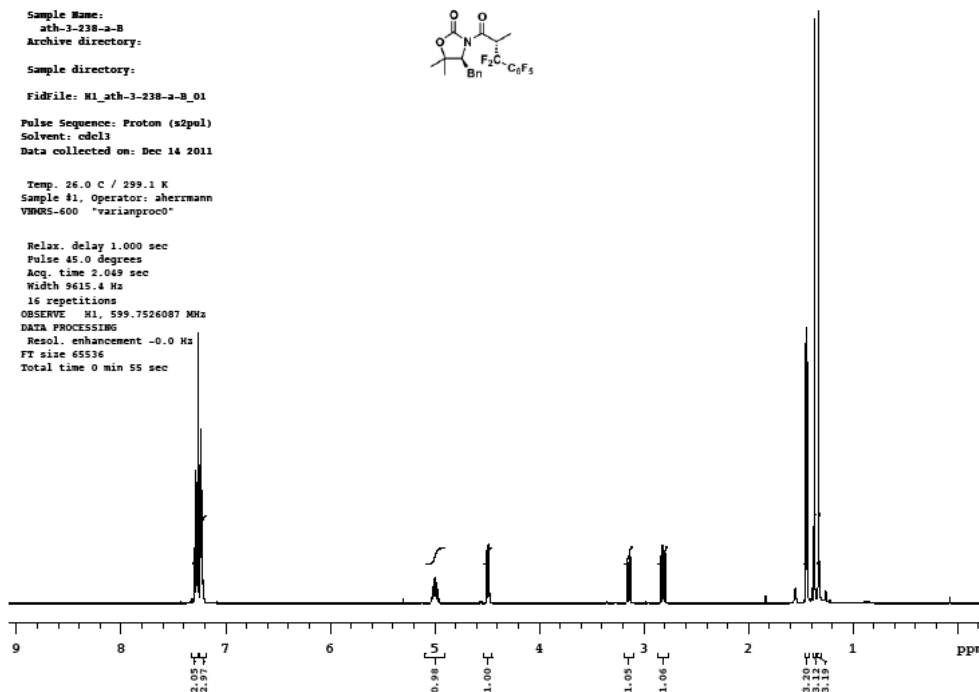
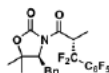
19F
600 MHz

Sample Name:
cmpd18
Archive directory:
Sample directory:
Fidfile: F19_cmpd18_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011
Temp. 26.0 C / 299.1 K
Sample #12, Operator: sherrmann
VNMRS-600 "varianproc0"

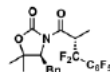


C13 NMR
600MHz

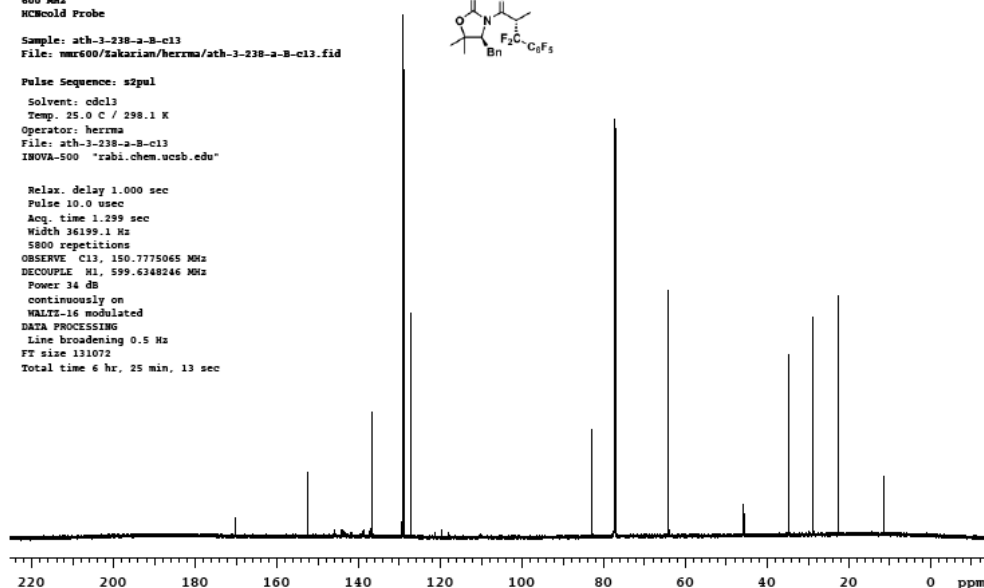
Sample Name:
ath-3-238-a-B
Archive directory:
Sample directory:
Fidfile: M1_ath-3-238-a-B_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 14 2011
Temp. 24.0 C / 299.1 K
Sample 41. Operator: ahermann
VNMR5-600 "varianproc5"



ath-3-238-a-B-c13
600 MHz
MCMold Probe
Sample: ath-3-238-a-B-c13
File: nmr600/Hakarian/herrma/ath-3-238-a-B-c13.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: herrma
File: ath-3-238-a-B-c13
INNOVA-500 "rabi.chem.ucsb.edu"



Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
5800 repetitions
OBSERVE C13, 150.7775065 MHz
DECOUPLE H1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec



C13 NMR
600MHz

Sample Name:
ath-3-238-a-B

Archive directory:

Sample directory:

Fidfile: F19_ath-3-238-a-B_01

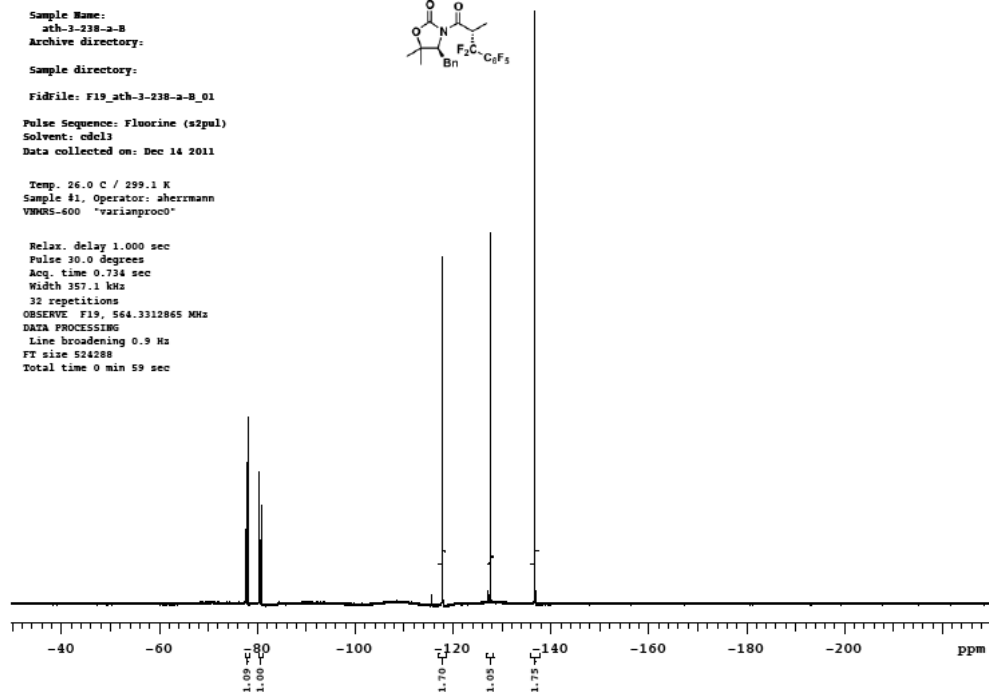
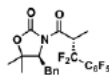
Pulse Sequence: Fluorine (s2pul)

Solvent: cdcl3

Data collected on: Dec 14 2011

Temp. 26.0 C / 299.1 K
Sample #1, Operator: aherrmann
VNMRS-600 "varianproc0"

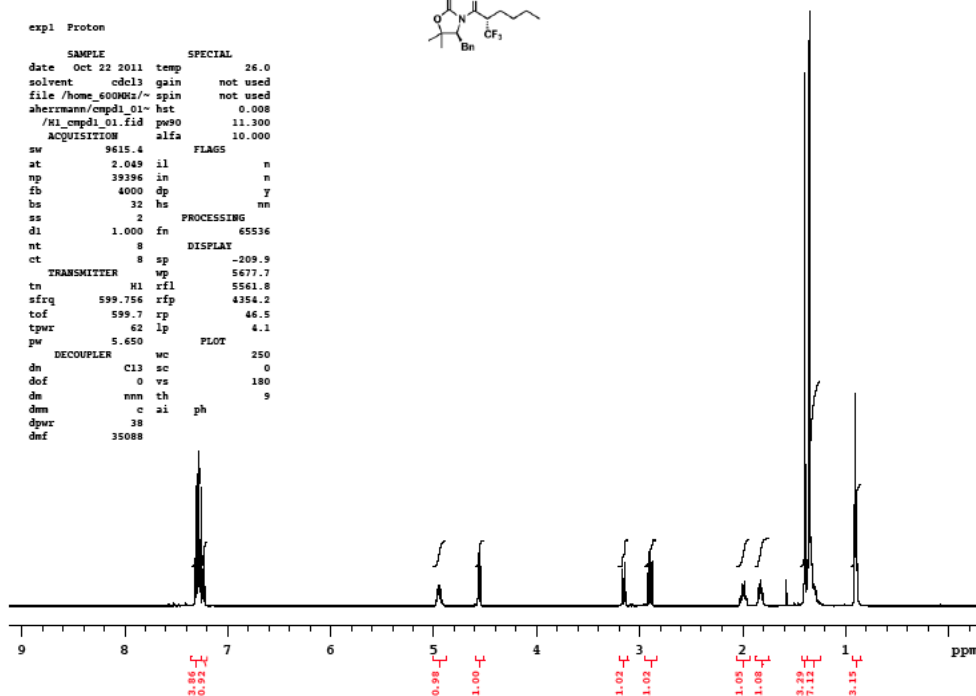
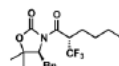
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 0.734 sec
Width 357.1 kHz
32 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 524288
Total time 0 min 59 sec



cmpd1
ath-3-143-a
600 MHz

expt Proton

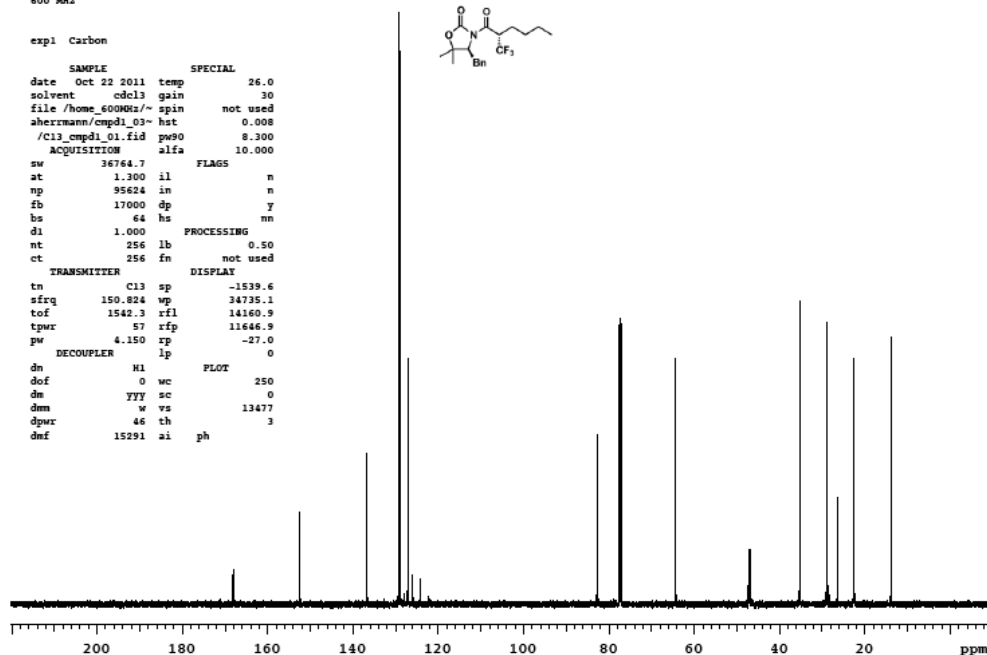
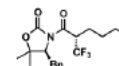
SAMPLE		SPECIAL	
date	Oct 22 2011	temp	26.0
solvent	cdcl3	gain	not used
file	/home_600MHz/~	spin	not used
sherrmann/cmpd1_01	hst		0.008
/N1_cmpd1_01.fid	pw90		11.300
ACQUISITION		alfa	10.000
sw	9615.4	FLAGS	
at	2.049	il	n
np	39396	in	n
fb	4000	dp	y
bs	32	hs	mn
ss	2	PROCESSING	
dl	1.000	fn	65536
nt	8	DISPLAY	
ct	8	sp	-209.9
TRANSMITTER		wp	5677.7
tn	N1	rfl	5561.8
sfrq	599.756	rpf	4354.2
tof	599.7	rp	46.5
tpwr	62	lp	4.1
pw	5.650	PLOT	
DECOUPLER		wc	250
dn	C13	sc	0
dof	0	vs	180
dm	nmn	th	9
dmm	c	ai	ph
dpwr	38		
dmf	35088		



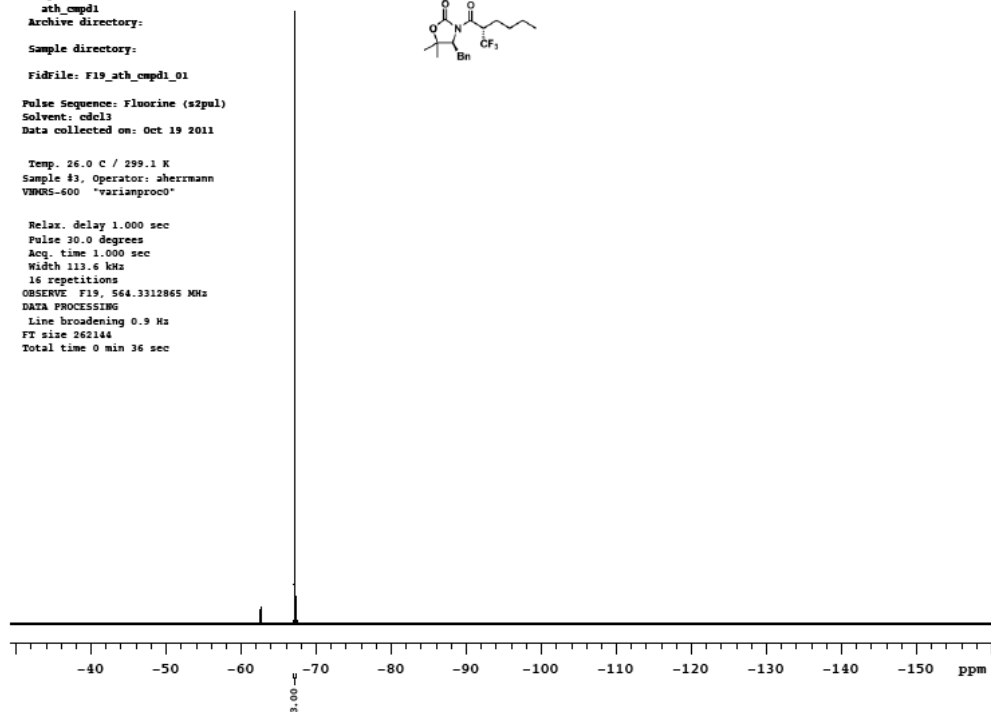
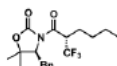
cmpd1
13C
ath-3-143-a
600 MHz

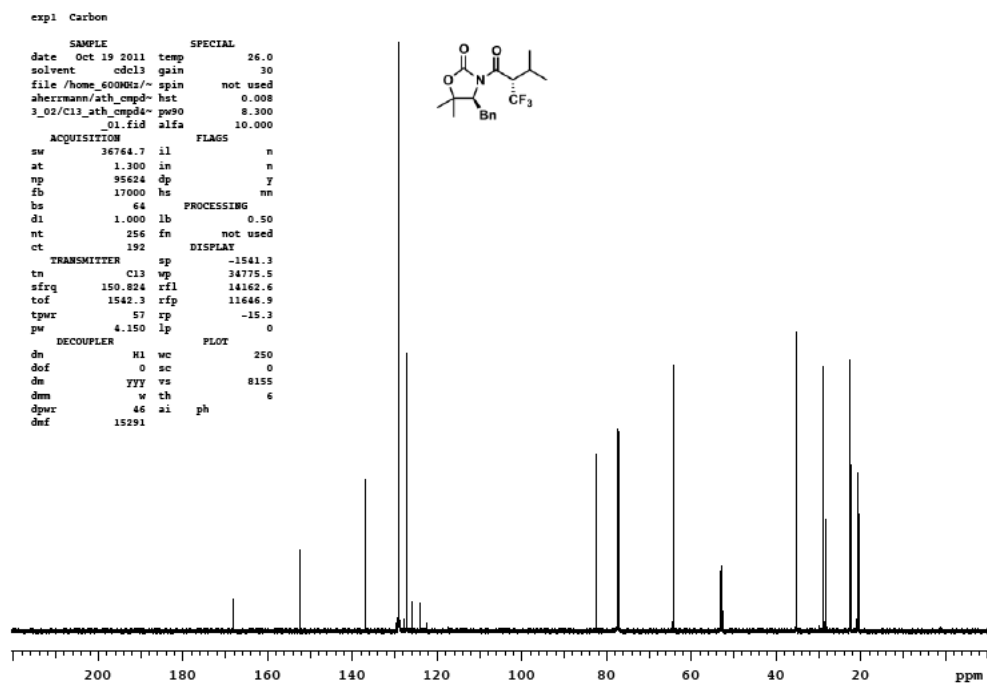
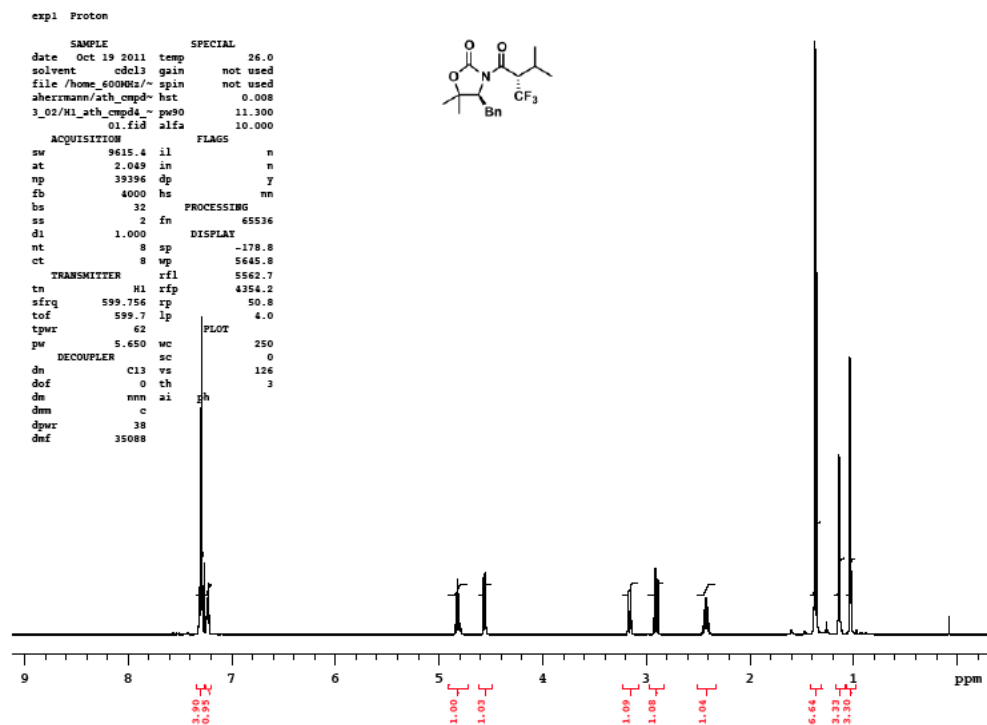
expt Carbon

SAMPLE		SPECIAL	
date	Oct 22 2011	temp	26.0
solvent	cdcl3	gain	30
file	/home_600MHz/~	spin	not used
sherrmann/cmpd1_03	hst		0.008
/C13_cmpd1_01.fid	pw90		8.300
ACQUISITION		alfa	10.000
sw	36764.7	FLAGS	
at	1.300	il	n
np	95624	in	n
fb	17000	dp	y
bs	64	hs	mn
dl	1.000	PROCESSING	
nt	256	lb	0.50
ct	256	fn	not used
TRANSMITTER		DISPLAY	
tn	C13	sp	-1539.6
sfrq	150.824	vp	34735.1
tof	1542.3	rfl	14160.9
tpwr	57	rpf	11646.9
pw	4.150	rp	-27.0
DECOUPLER		lp	0
dn	N1	PLOT	
dof	0	wc	250
dm	YYY	sc	0
dmm	w	vs	13477
dpwr	46	th	3
dmf	15291	ai	ph

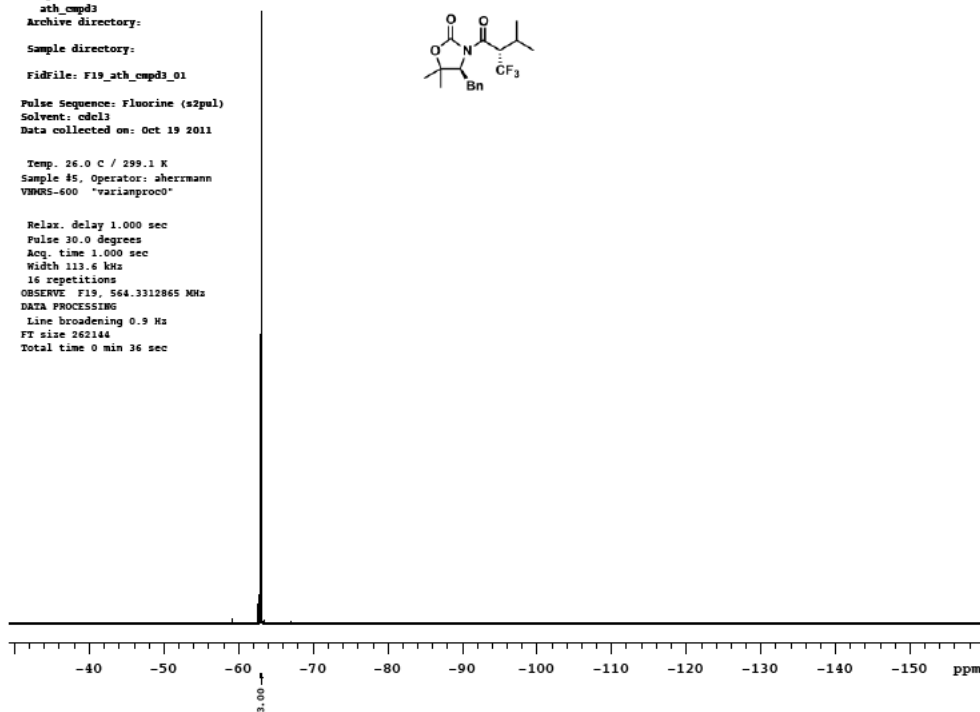
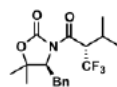


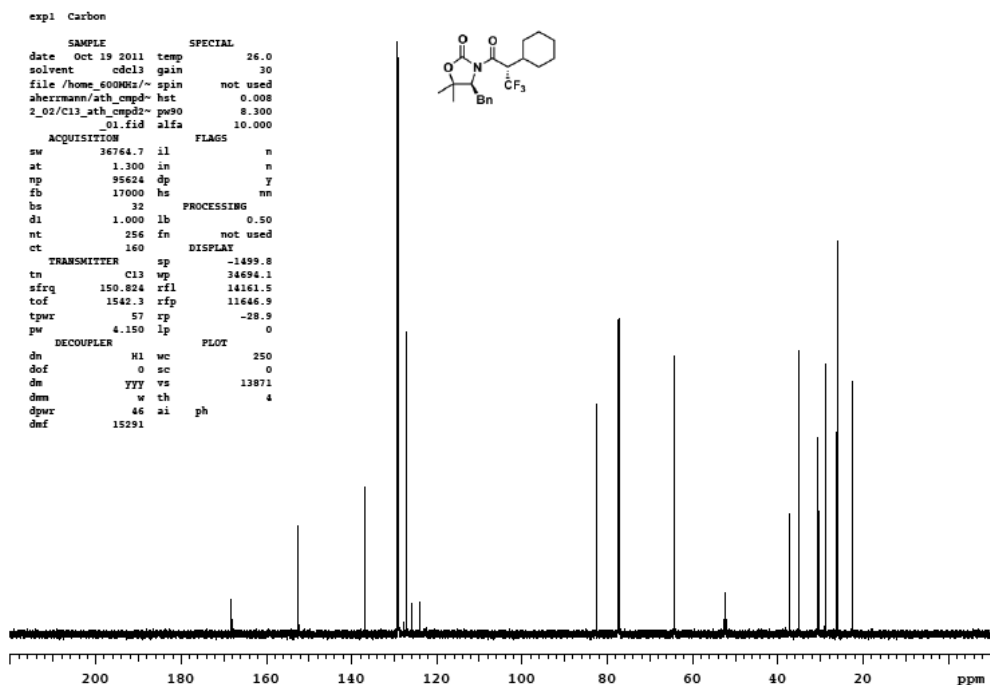
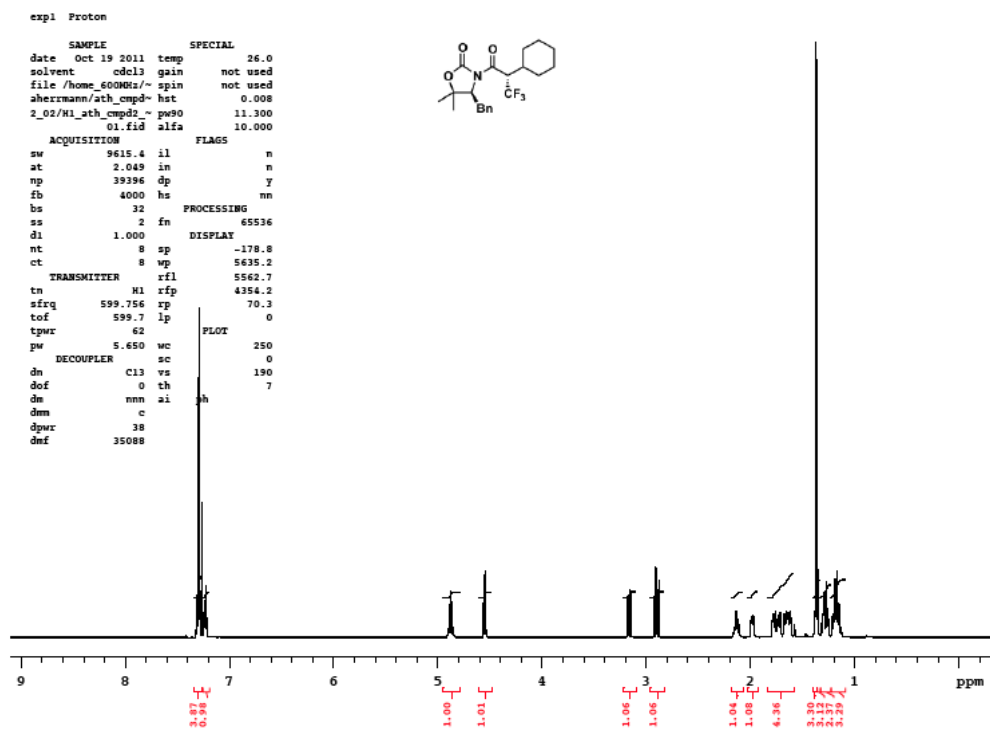
Sample Name:
 ath_comp1
 Archive directory:
 Sample directory:
 F19_ath_comp1_01
 Pulse Sequence: Fluorine (s2gsl)
 Solvent: cdcl3
 Data collected on: Oct 19 2011
 Temp. 26.0 C / 299.1 K
 Sample 43, Operator: sherrmann
 VNMRS-600 "varianproc0"
 Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 1.000 sec
 Width 113.6 kHz
 16 repetitions
 OBSERVE F19, 564.3312865 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 262144
 Total time 0 min 36 sec



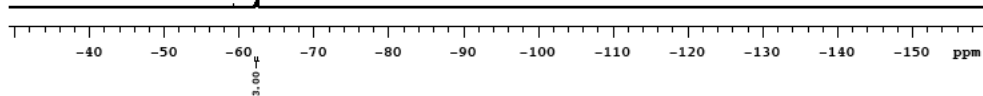
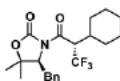


Sample Name:
 ath_comp3
 Archive directory:
 Sample directory:
 FidFile: F19_ath_comp3_01
 Pulse Sequence: Fluorine (s2pul)
 Solvent: cdcl3
 Data collected on: Oct 19 2011
 Temp. 26.0 C / 299.1 K
 Sample #5, Operator: aherrmann
 VNMRS-600 "varianproc0"
 Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 1.000 sec
 Width 113.6 kHz
 16 repetitions
 OBSERVE F19, 564.3312865 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 262144
 Total time 0 min 36 sec





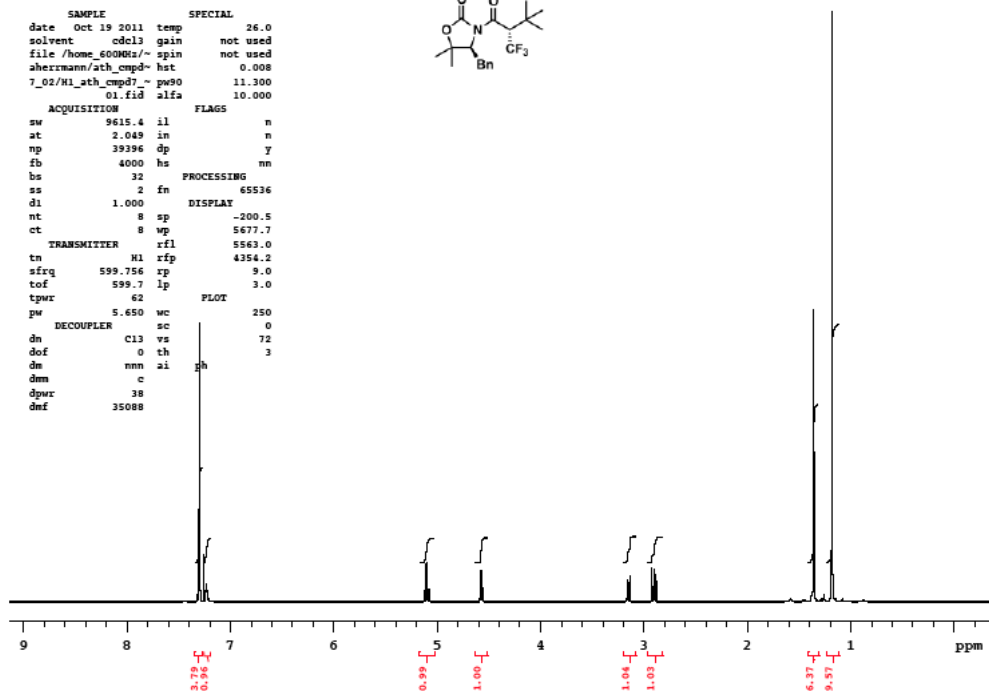
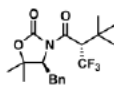
Sample Name:
 ath_comp2
 Archive directory:
 Sample directory:
 FIDfile: F19_ath_comp2_01
 Pulse Sequence: Fluorine (s2pul)
 Solvent: cdcl3
 Data collected on: Oct 19 2011
 Temp. 26.0 C / 299.1 K
 Sample #4. Operator: aherrmann
 VNMRS-600 "varianproco"
 Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 1.000 sec
 Width 113.6 kHz
 16 repetitions
 OBSERVE F19, 564.3312865 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 262144
 Total time 0 min 36 sec



expl Proton

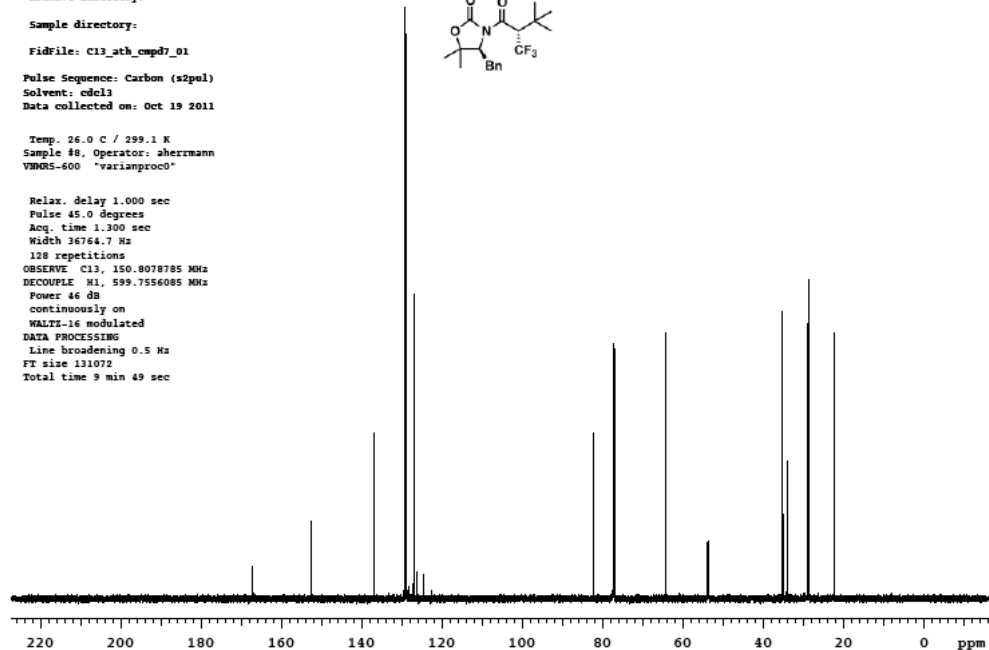
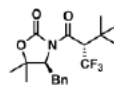
SAMPLE SPECIAL
 date Oct 19 2011 temp 26.0
 solvent cdcl3 gain not used
 file /home_600MHz/~ spin not used
 aherrmann/ath_cmpd7-hst 0.008
 7_02/H1_ath_cmpd7_- pw90 11.300
 01.fid alfa 10.000

ACQUISITION FLAGS
 sw 9615.4 il n
 at 2.049 in n
 np 39396 dp y
 fb 4000 hs nm
 bs 32
 ss 2 fn PROCESSING 65536
 dl 1.000 DISPLAY
 nt 8 sp -200.5
 ct 8 wp 5677.7
 TRANSMITTER
 tn H1 rfp 4354.2
 sfrq 599.756 rp 9.0
 tof 599.7 lp 3.0
 tpwr 62
 pw 5.650 wc PLOT 250
 DECOUPLER sc 0
 dn C13 vs 72
 dof 0 th 3
 ds nm ai ph
 dm c
 dpwr 38
 dmf 35088

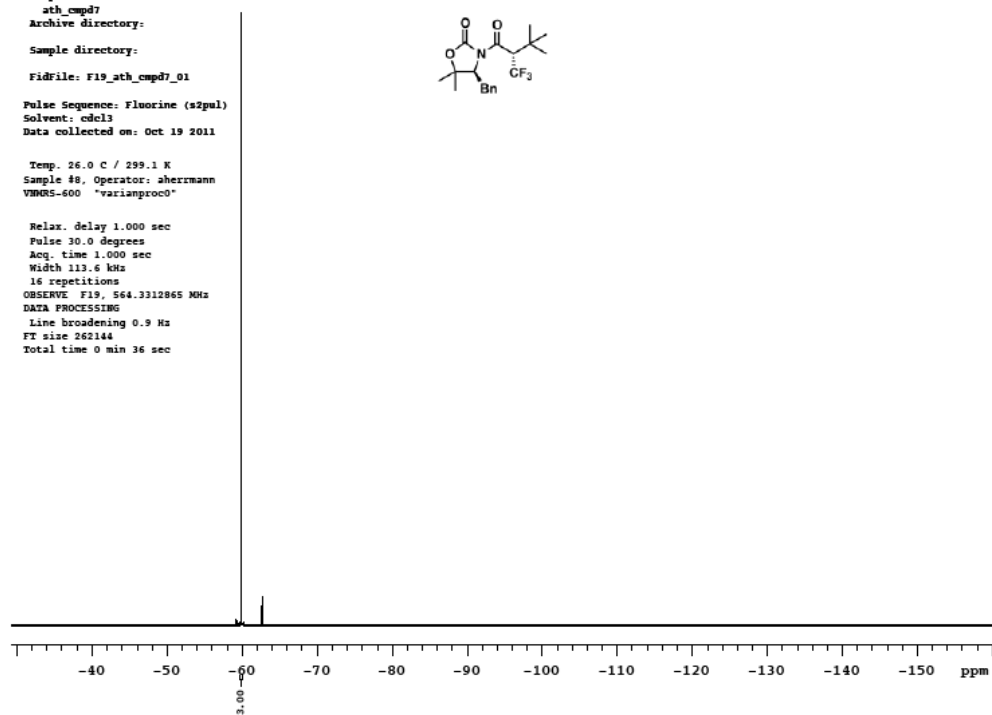
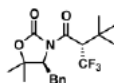


Sample Name:
 ath_cmpd7
 Archive directory:
 Sample directory:
 Fidfile: C13_ath_cmpd7_01
 Pulse Sequence: Carbon (s2pul)
 Solvent: cdcl3
 Data collected on: Oct 19 2011

Temp. 26.0 C / 299.1 K
 Sample 48, Operator: aherrmann
 VNMR5-600 "varianproc0"

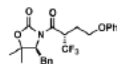


Sample Name:
 ath_comp7
 Archive directory:
 Sample directory:
 Fidfile: F19_ath_comp7_01
 Pulse Sequence: Fluorine (s2pul)
 Solvent: cdcl3
 Data collected on: Oct 19 2011
 Temp. 26.0 C / 299.1 K
 Sample 48, Operator: sherrmann
 VNMRS-600 "varianproc0"
 Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 1.000 sec
 Width 113.6 kHz
 16 repetitions
 OBSERVE F19, 564.3312865 MHz
 DATA PROCESSING
 Line broadening 0.9 Hz
 FT size 262144
 Total time 0 min 36 sec



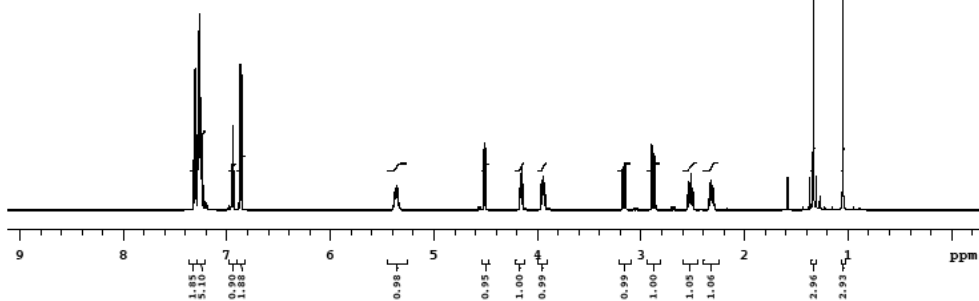
ath-3-166-a
600 MHz

Sample Name:
cmpd10
Archive directory:
Sample directory:
FidFile: M1_cmpd10_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011



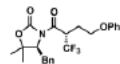
Temp. 26.0 C / 299.1 K
Sample #8, Operator: ahermann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 Degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE M1, 599.7526151 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 9 min 30 sec



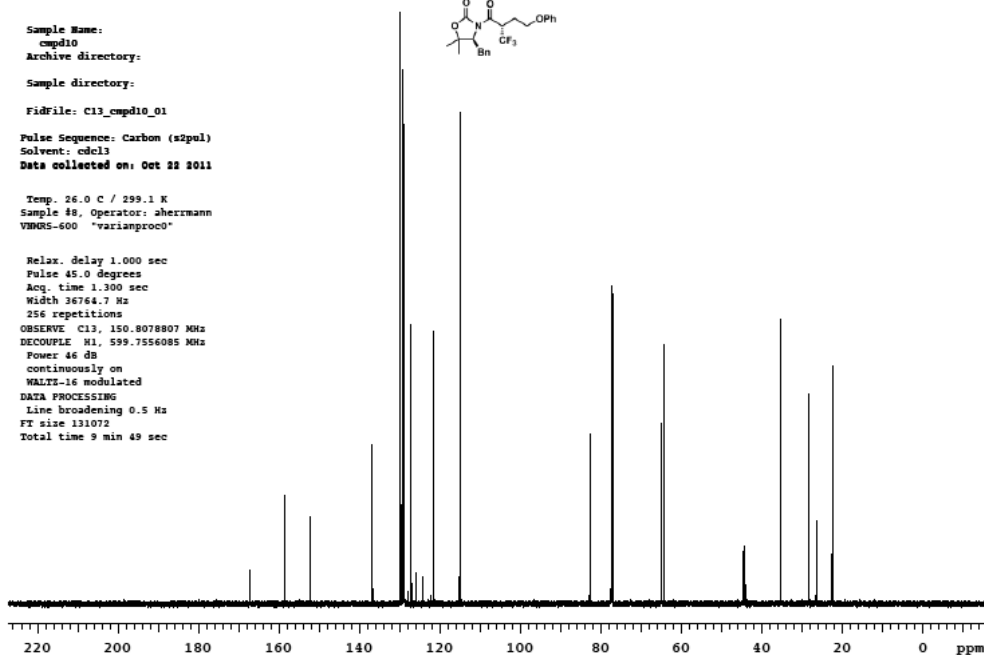
13C
ath-3-166-a
600 MHz

Sample Name:
cmpd10
Archive directory:
Sample directory:
FidFile: C13_cmpd10_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011



Temp. 26.0 C / 299.1 K
Sample #8, Operator: ahermann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
256 repetitions
OBSERVE C13, 150.8078807 MHz
DECOUPLE M1, 599.7556085 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min 49 sec

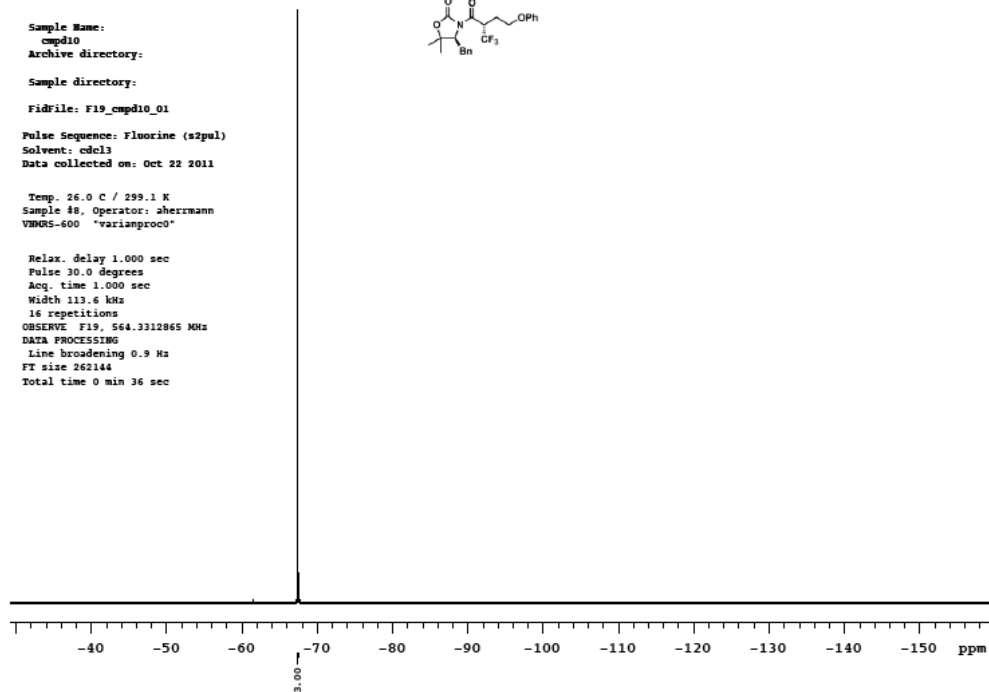
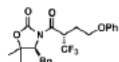


19F
ath-3-166-a
600 MHz

Sample Name:
cmpd10
Archive directory:
Sample directory:
Fidfile: F19_cmpd10_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011

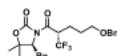
Temp. 26.0 C / 299.1 K
Sample 48, Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec

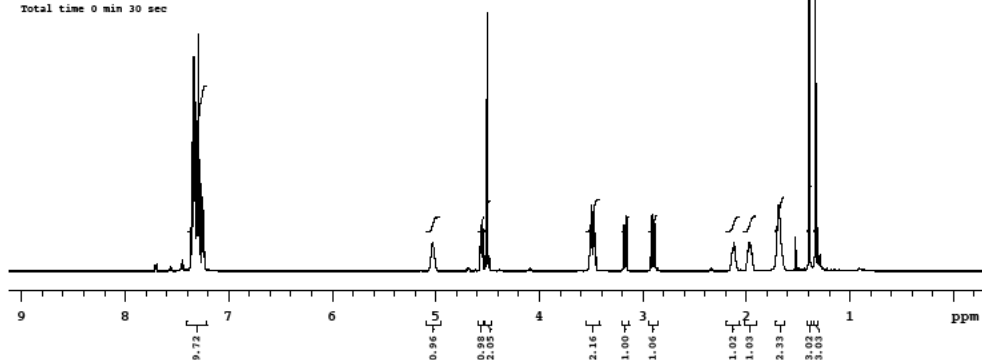


1H

Sample Name:
cmpd9
Archive directory:
Sample directory:
FidFile: H1_cmpd9_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011

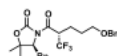


Temp. 26.0 C / 299.1 K
Sample #8, Operator: ahermann
VNMRS-600 "varianproco"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE H1, 599.7526072 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec

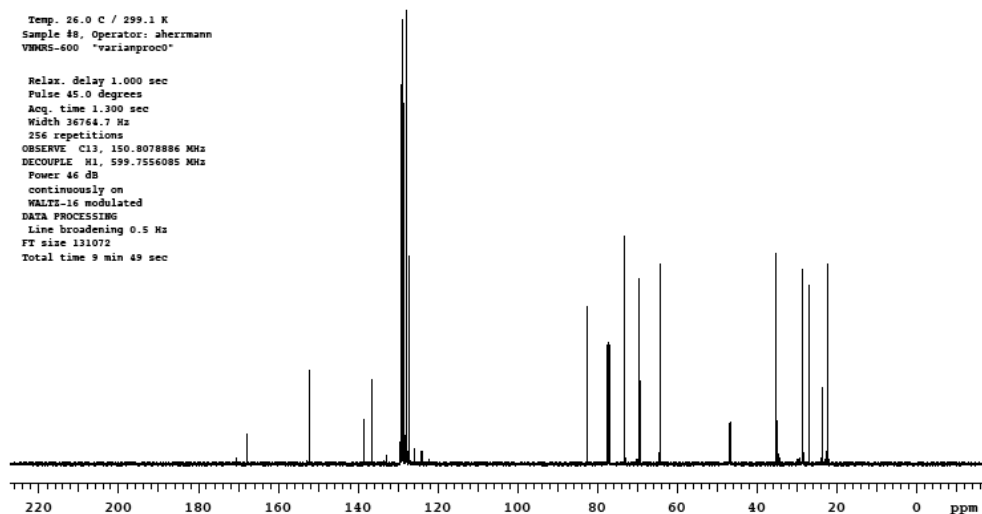


13C

Sample Name:
cmpd9
Archive directory:
Sample directory:
FidFile: C13_cmpd9_01
Pulse Sequence: Carbon (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011



Temp. 26.0 C / 299.1 K
Sample #8, Operator: ahermann
VNMRS-600 "varianproco"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 36764.7 Hz
256 repetitions
OBSERVE C13, 150.8078886 MHz
DECOUPLE H1, 599.7556085 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 9 min 49 sec

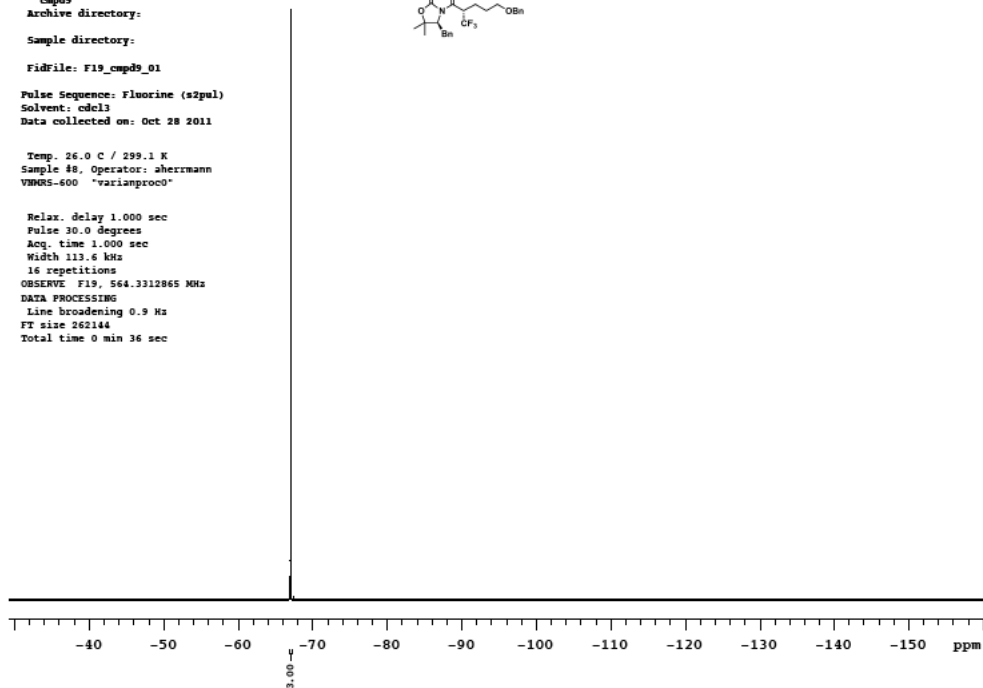
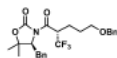


19F

Sample Name:
comp9
Archive directory:
Sample directory:
FidFile: F19_comp9_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011

Temp. 26.0 C / 299.1 K
Sample #8, Operator: aherrmann
VNMRS-600 "varianproc0"

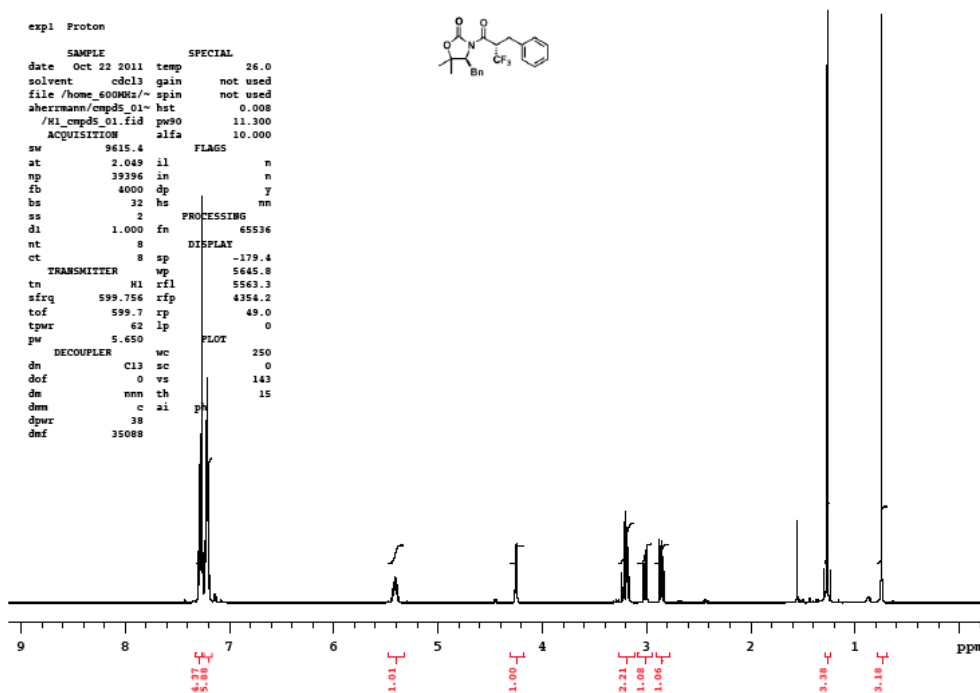
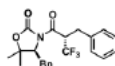
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 119.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



cmpd5
ath-3-1159-a
600 MHz

expt1 Proton

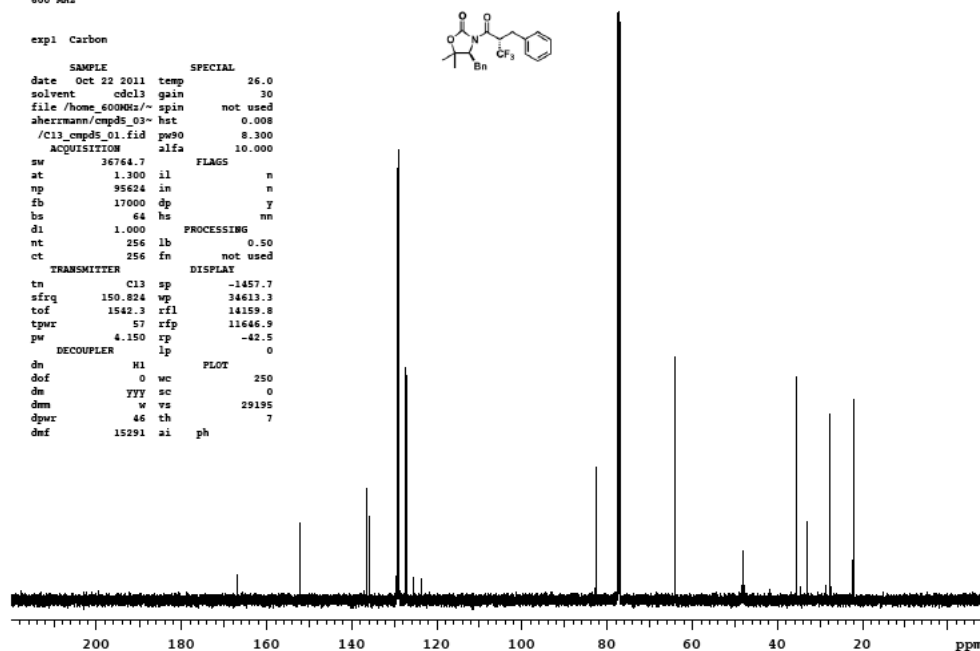
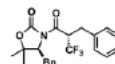
SAMPLE		SPECIAL	
date	Oct 22 2011	temp	26.0
solvent	cdcl3	gain	not used
file	/home_600MHz/~	spin	not used
aherrmann/cmpd5_01	hst		0.008
/H1_cmpd5_01.fid	pw90		11.300
ACQUISITION	alfa		10.000
sw	9615.4	FLAGS	
at	2.049	il	n
np	39396	in	n
fb	4000	dp	y
bs	32	hs	mn
ss	2	PROCESSING	
di	1.000	fn	65536
nt	8	DISPLAY	
ct	8	sp	-179.4
TRANSMITTER	wp		5645.8
tn	H1	rfl	5563.3
sfrq	599.756	rfp	4354.2
tof	599.7	rp	49.0
tpwr	62	lp	0
pw	5.650	PLOT	
DECOUPLER	wc		250
dn	C13	sc	0
dof	0	vs	143
dm	nnn	th	15
dmm	c	ai	
dpwr	38		
dmf	35088		



cmpd5
13C
ath-3-159-a
600 MHz

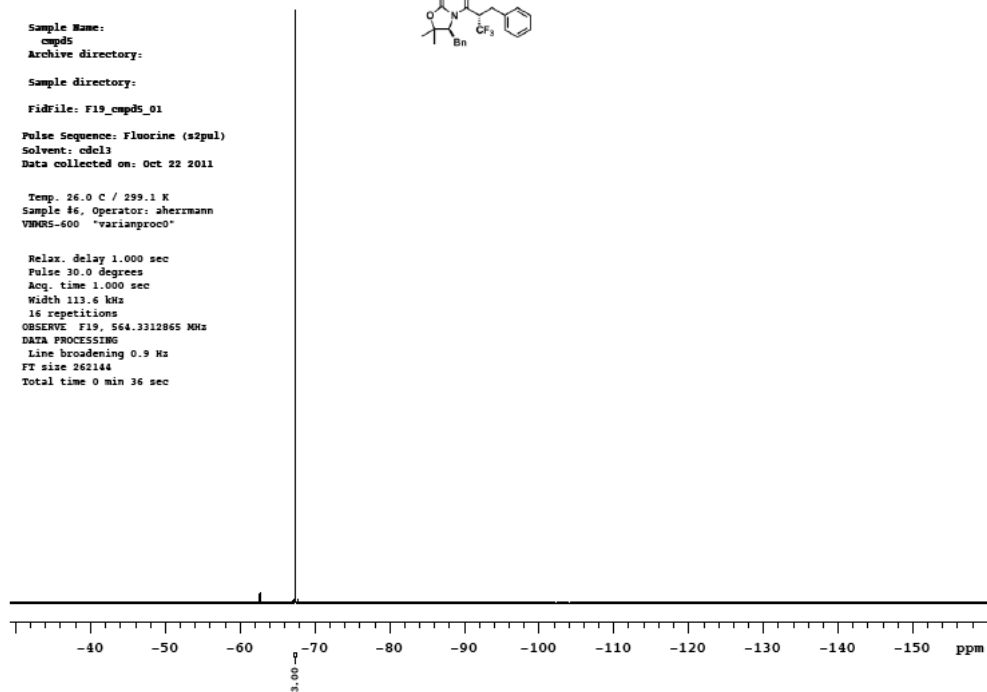
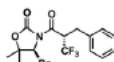
expt1 Carbon

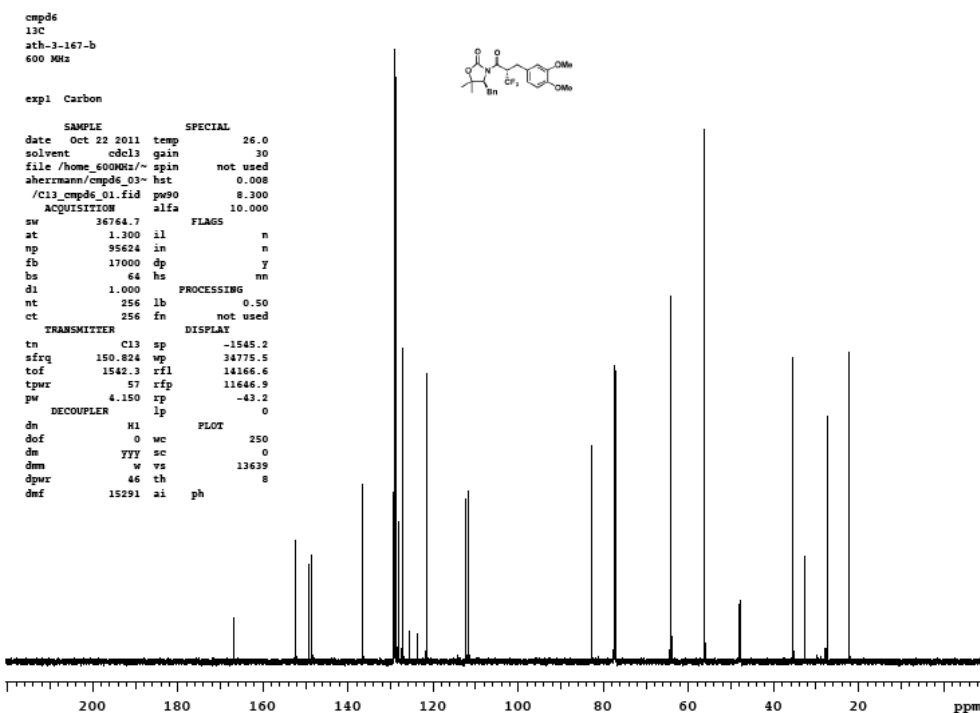
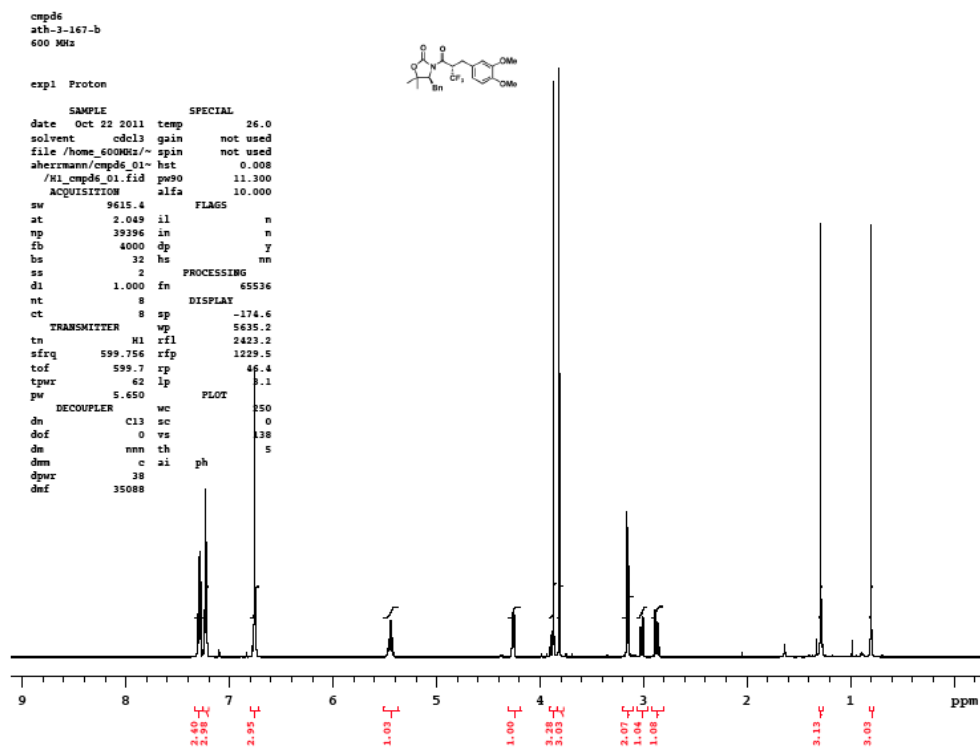
SAMPLE		SPECIAL	
date	Oct 22 2011	temp	26.0
solvent	cdcl3	gain	30
file	/home_600MHz/~	spin	not used
aherrmann/cmpd5_03	hst		0.008
/C13_cmpd5_01.fid	pw90		8.300
ACQUISITION	alfa		10.000
sw	36764.7	FLAGS	
at	1.300	il	n
np	95624	in	n
fb	17000	dp	y
bs	64	hs	mn
di	1.000	PROCESSING	
nt	256	lb	0.50
ct	256	fn	not used
TRANSMITTER		DISPLAY	
tn	C13	sp	-1457.7
sfrq	150.824	wp	34613.3
tof	1542.3	rfl	14159.8
tpwr	57	rfp	11646.9
pw	4.150	lp	-42.5
DECOUPLER			0
dn	H1	PLOT	
dof	0	wc	250
dm	YYY	sc	0
dmm	w	vs	29195
dpwr	46	th	7
dmf	15291	ai	ph



19F
ath-3-159-a
600 MHz

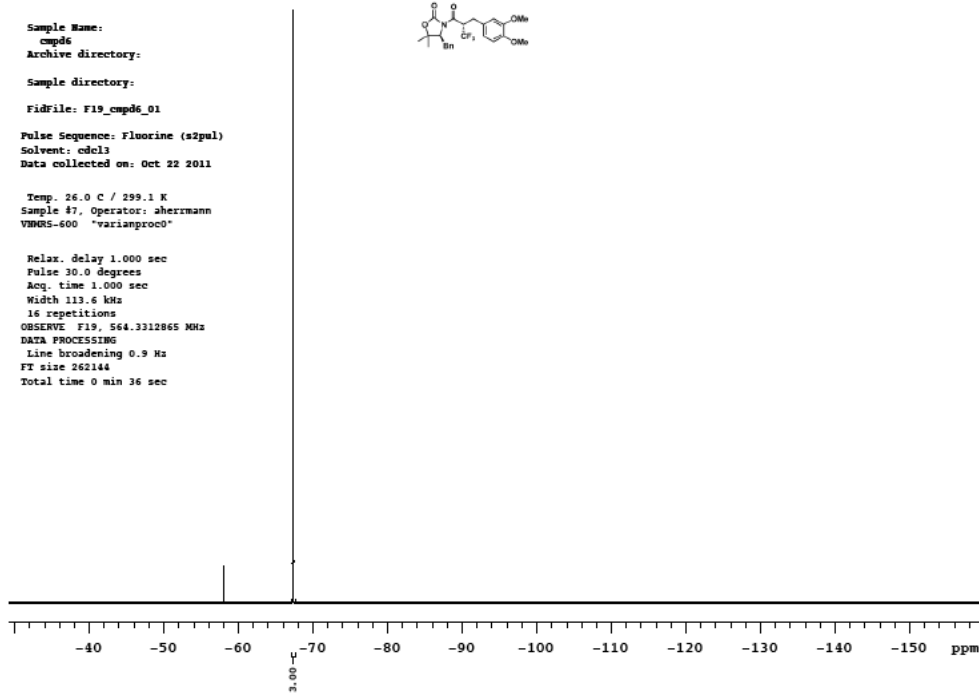
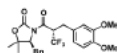
Sample Name:
comp5
Archive directory:
Sample directory:
FidFile: F19_comp5_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011
Temp. 26.0 C / 299.1 K
Sample 46, Operator: aherrmann
VNMRS-600 "varianproc0"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec





19F
ath-3-167-b
600 MHz

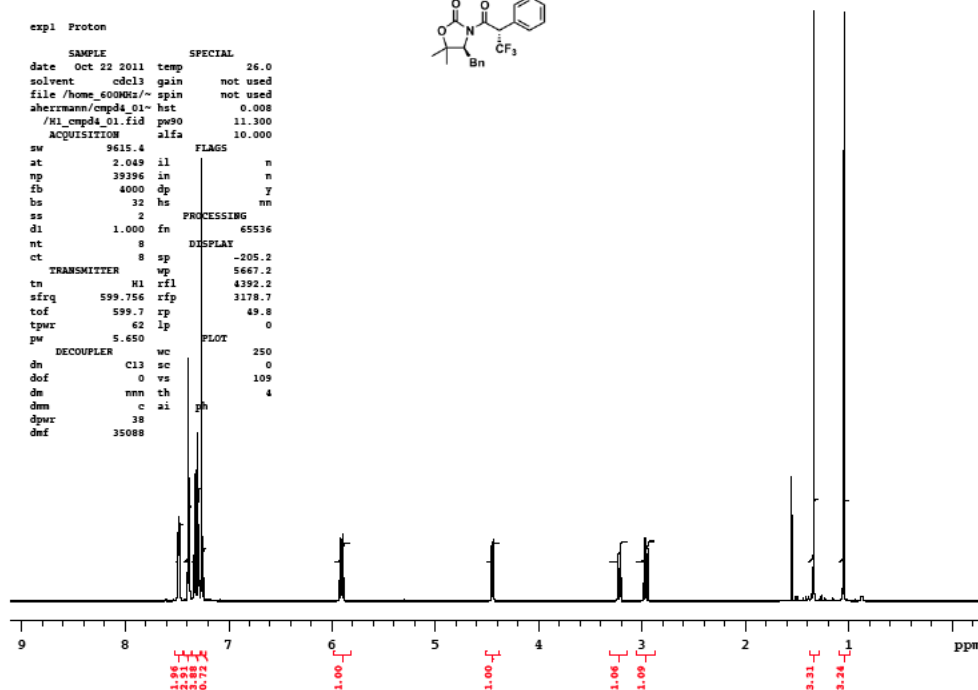
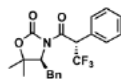
Sample Name:
cmpd6
Archive directory:
Sample directory:
FidFile: F19_cmpd6_01
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011
Temp. 26.0 C / 299.1 K
Sample #7, Operator: ahermann
VNMR5-600 "varianproc0"
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



cmpd4
ath-3-132-a
600 MHz

expt1 Proton

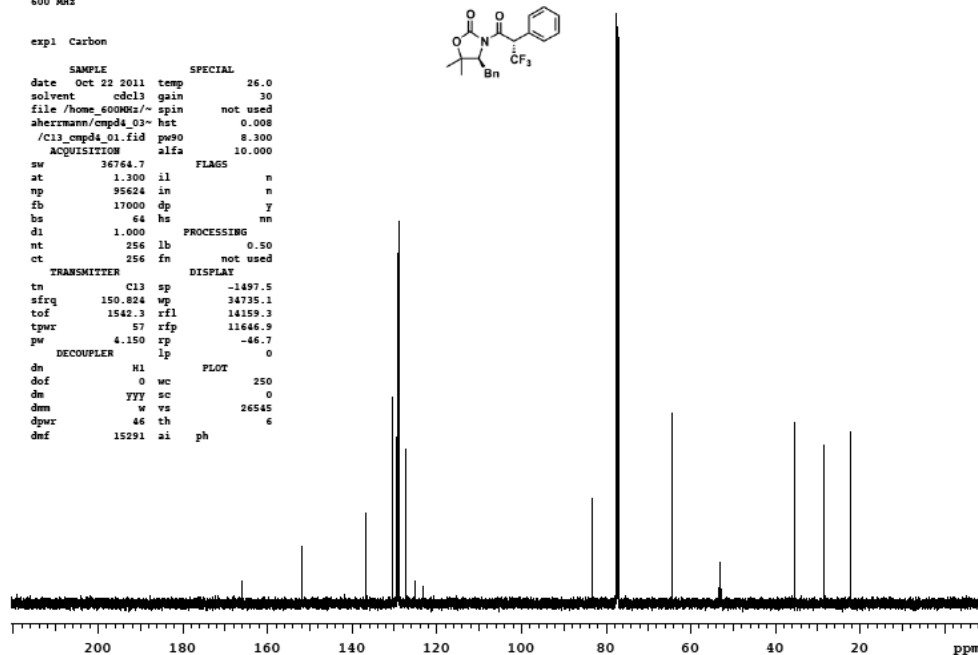
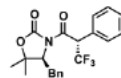
SAMPLE		SPECIAL	
date	Oct 22 2011	temp	26.0
solvent	cdcl3	gain	not used
file	/home_600MHz/~ spin	not used	
sherrmann/cmpd4_01~	hst	0.008	
/H1_cmpd4_01.fid	pw90	11.300	
ACQUISITION	alfa	10.000	
sw	9615.4	FLAGS	
at	2.049	il	n
np	39396	in	n
fb	4000	dp	y
bs	32	hs	nn
ss	2	PROCESSING	
dl	1.000	fn	65536
nt	8	DISPLA	
ct	8	sp	-205.2
TRANSMITTER	wp	5667.2	
tn	H1	rfl	4392.2
sfrq	599.756	rpf	3178.7
tof	599.7	rp	49.8
tpwr	62	lp	0
pw	5.650	PLOT	
DECOUPLER	wc	250	
dn	C13	sc	0
dof	0	vs	109
dm	nnn	th	4
dmm	c	ai	
dpwr	38		
dmf	35088		



cmpd4
13C
ath-3-132-a
600 MHz

expt1 Carbon

SAMPLE		SPECIAL	
date	Oct 22 2011	temp	26.0
solvent	cdcl3	gain	30
file	/home_600MHz/~ spin	not used	
sherrmann/cmpd4_03~	hst	0.008	
/C13_cmpd4_01.fid	pw90	8.300	
ACQUISITION	alfa	10.000	
sw	36764.7	FLAGS	
at	1.300	il	n
np	95624	in	n
fb	17000	dp	y
bs	64	hs	nn
dl	1.000	PROCESSING	
nt	256	lb	0.50
ct	256	fn	not used
TRANSMITTER	sp	DISPLAY	
tn	C13	sp	-1497.5
sfrq	150.824	wp	34735.1
tof	1542.3	rfl	14159.3
tpwr	57	rpf	11646.9
pw	4.150	rp	-46.7
DECOUPLER	lp	0	
dn	H1	PLOT	
dof	0	wc	250
dm	YYY	sc	0
dmm	w	vs	26545
dpwr	46	th	6
dmf	15291	ai	ph



19F
ath-3-132-a
600 MHz

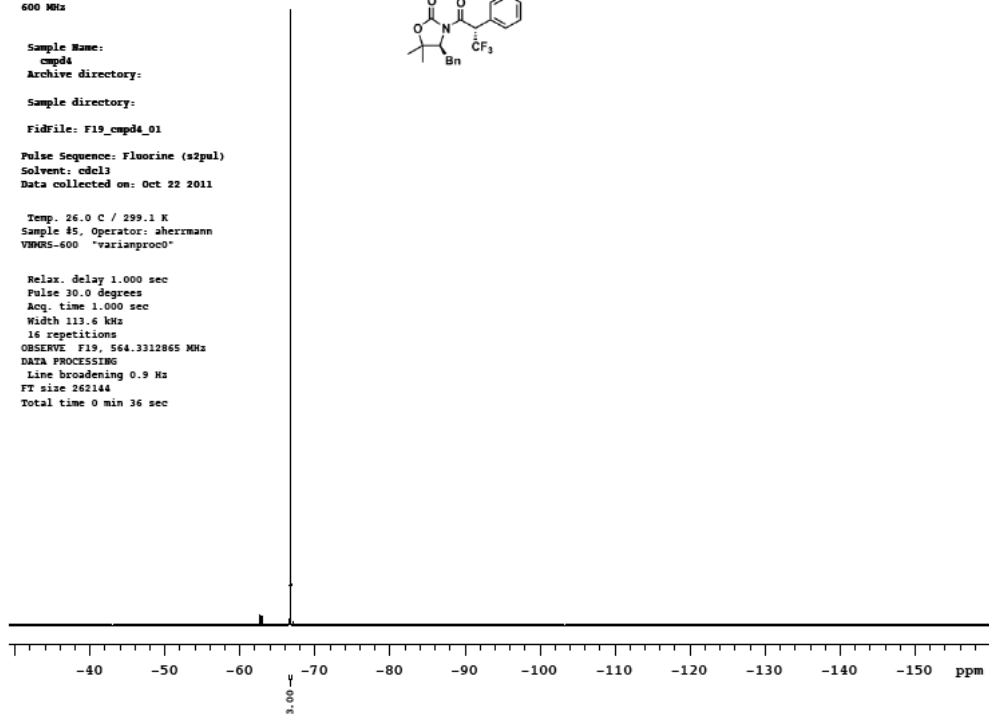
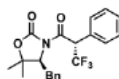
Sample Name:
comp4
Archive directory:

Sample directory:
FidFile: F19_comp4_01

Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 22 2011

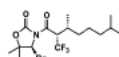
Temp. 26.0 C / 299.1 K
Sample 45, Operator: aherrmann
VMHRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



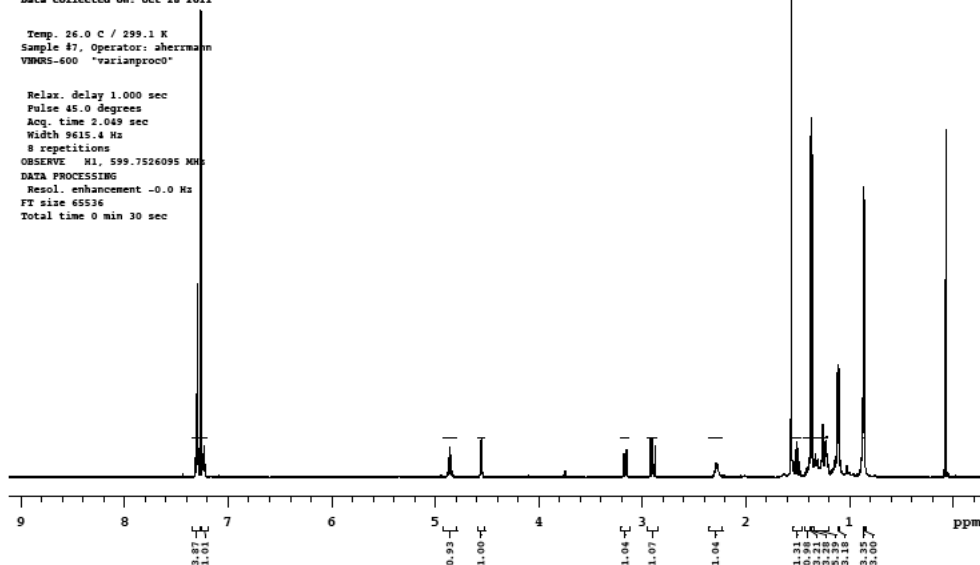
1H

Sample Name:
comp8
Archive directory:
Sample directory:

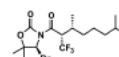


FidFile: M1_comp8_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011

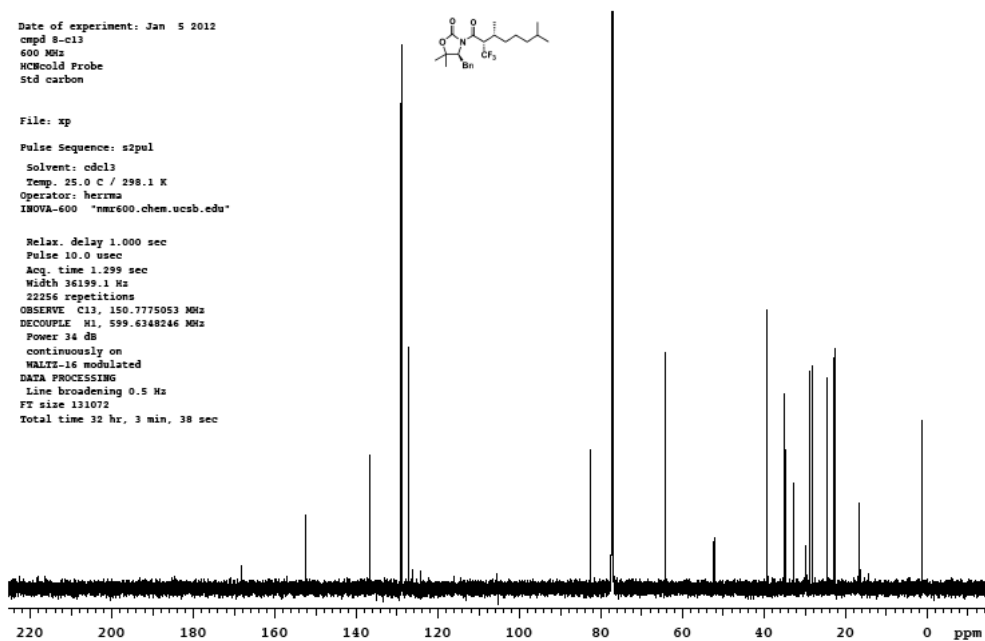
Temp. 26.0 C / 299.1 K
Sample #7, Operator: ahermann
VNMRS-600 "varianproco"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 9615.4 Hz
8 repetitions
OBSERVE M1, 599.7526095 MHz
DATA PROCESSING
Resol. enhancement -0.0 Hz
FT size 65536
Total time 0 min 30 sec



Date of experiment: Jan 5 2012
comp 8-cl3
600 MHz
MCRoid Probe
Std carbon



File: xp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: herma
INOVA-600 "nmr600.chem.ucsb.edu"
Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
22256 repetitions
OBSERVE C13, 150.7775053 MHz
DECOUPLE M1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 32 hr, 3 min, 38 sec



19F

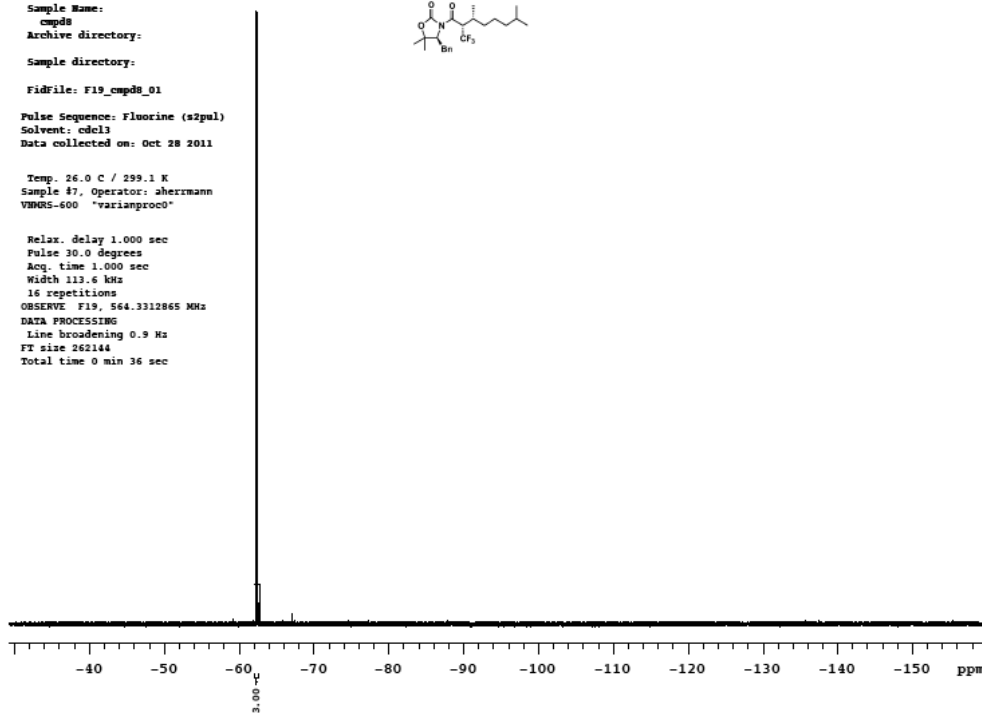
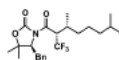
Sample Name:
cmpds
Archive directory:
Sample directory:

Fidfile: F19_cmpds_01

Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Oct 28 2011

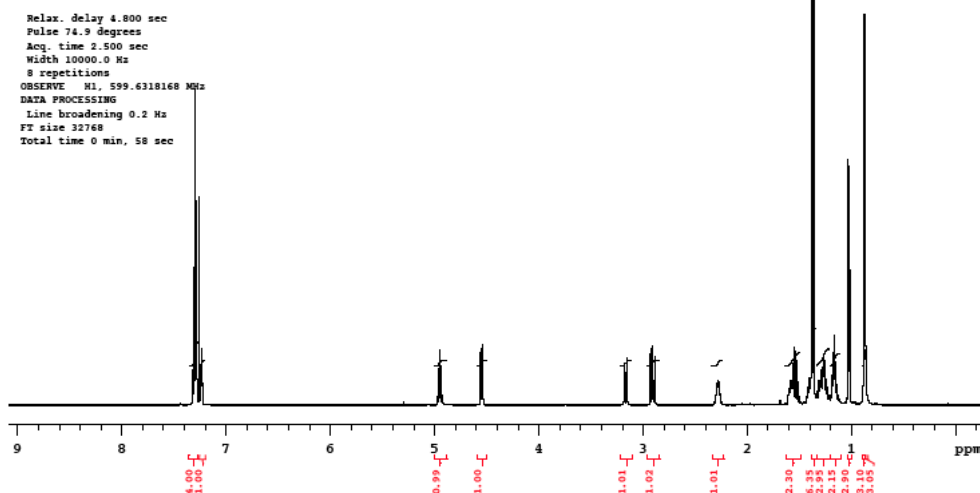
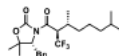
Temp. 26.0 C / 299.1 K
Sample 47, Operator: sherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



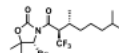
File: nmr600/Takarim/lsmith/vnmrsys/data/ath-3-203-p.fid

Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: lsmith
File: ath-3-203-p
INOVA-500 "rabi.chem.ucsb.edu"



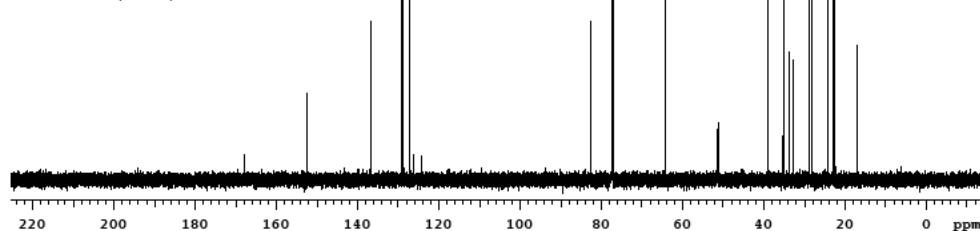
Std carbon

Sample: 1_Indanone
File: nmr600/Takarim/lsmith/vnmrsys/data/ath-3-203-p-carbon.fid



Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: lsmith
File: ath-3-203-p-carbon
INOVA-500 "rabi.chem.ucsb.edu"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
185 repetitions
OBSERVE C13, 150.7775065 MHz
DECOUPLE H1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 25 min, 13 sec



19F

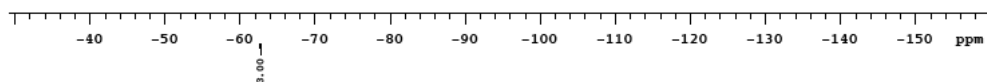
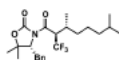
Sample Name:
ath-3-203-p
Archive directory:
Sample directory:

FidFile: F19_ath-3-203-p_01

Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Nov 7 2011

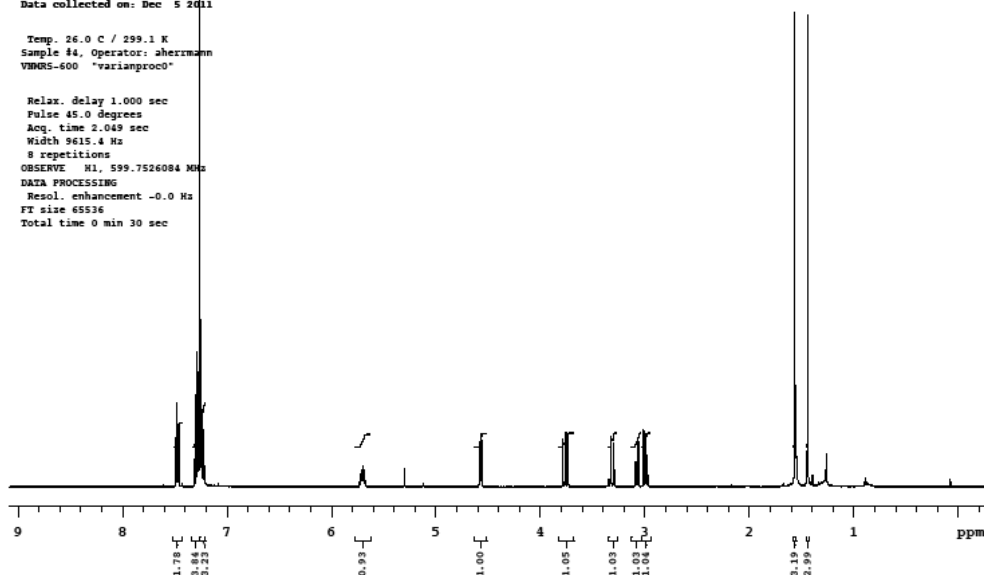
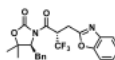
Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VNMRS-600 "varianproco"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



600MHz

Sample Name:
ath-3-240-a-a
Archive directory:
Sample directory:
Fidfile: N1_ath-3-240-a-a_01
Pulse Sequence: Proton (s2pul)
Solvent: cdcl3
Data collected on: Dec 5 2011



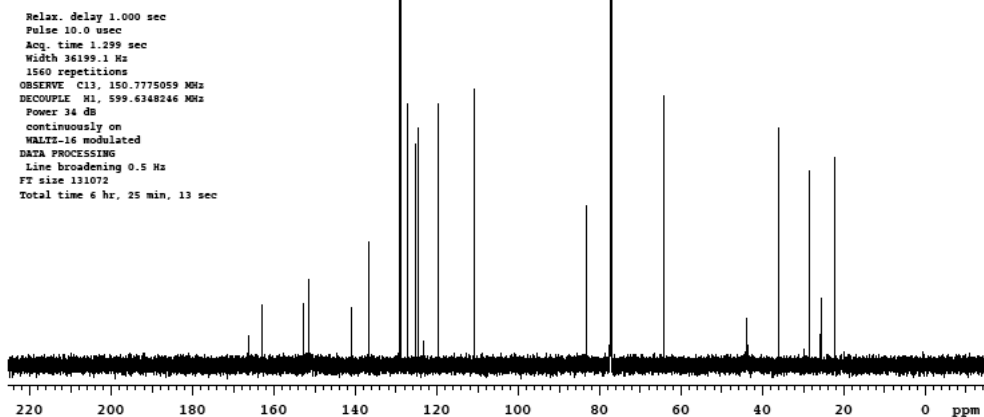
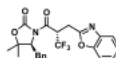
ath-3-240-a-a-c13

600MHz

NCH Probe

Sample: ath-3-240-a-a-c13
File: nm600/takarian/berrma/ath-3-240-a-a-c13.fid

Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: berrma
File: ath-3-240-a-a-c13
INOVA-500 "rabi.chem.ucsb.edu"



600MHz

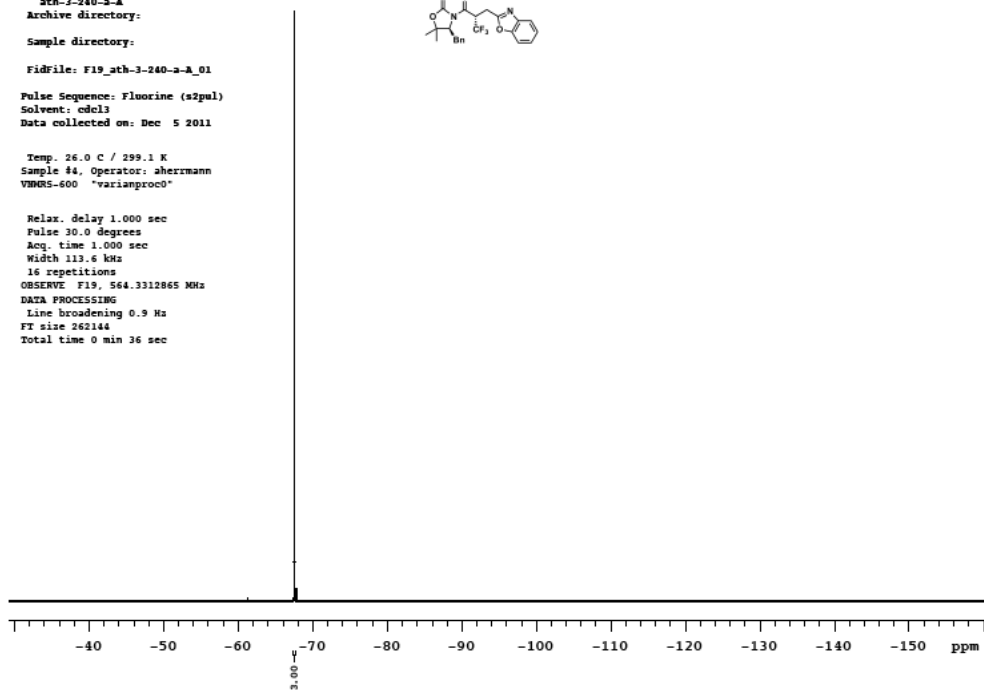
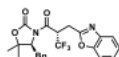
Sample Name:
ath-3-240-a-a
Archive directory:
Sample directory:

FidFile: F19_ath-3-240-a-a_01

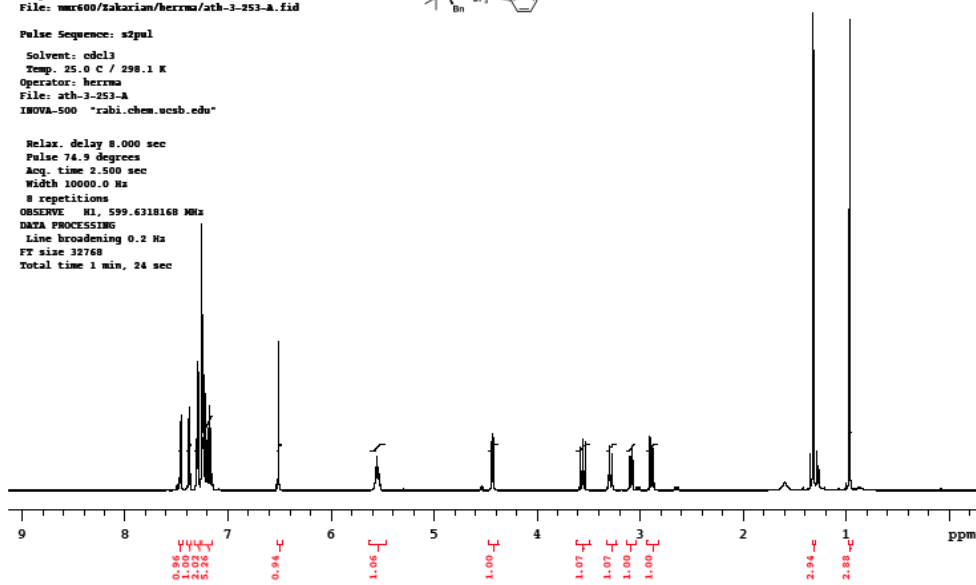
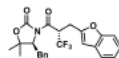
Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Dec 5 2011

Temp. 26.0 C / 299.1 K
Sample #4, Operator: ahermann
VNMRS-600 "varianproco"

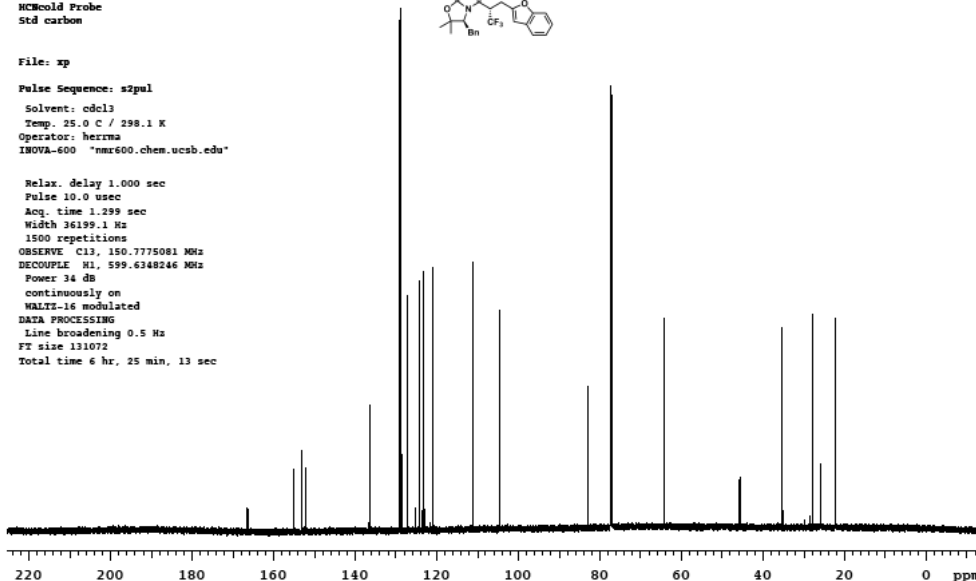
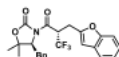
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



ath-3-253-A
600 MHz
HMCold Probe
Sample: ath-3-253-A
File: nmr600/takarima/herrma/ath-3-253-A.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: herrma
File: ath-3-253-A
INOVA-500 "rabi.chem.ucsb.edu"



Date of experiment: Jan 4 2012
ath-3-253-A-cl3
600 MHz
HMCold Probe
Std carbon
File: xp
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: herrma
INOVA-600 "nmr600.chem.ucsb.edu"



19F

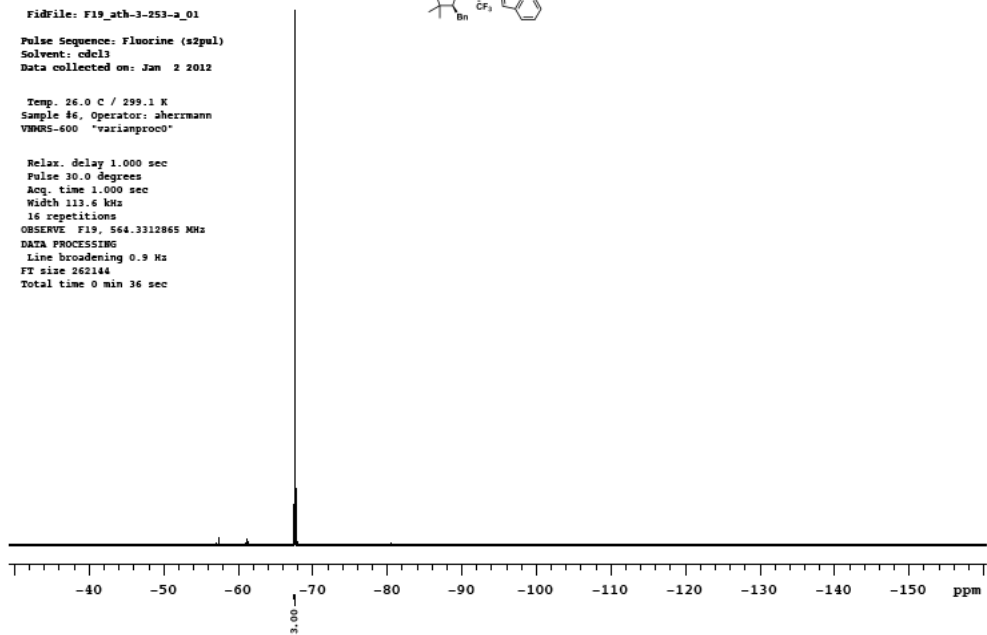
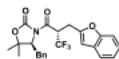
Sample Name:
ath-3-253-a
Archive directory:
Sample directory:

FidFile: F19_ath-3-253-a_01

Pulse Sequence: Fluorine (s2pul)
Solvent: cdcl3
Data collected on: Jan 2 2012

Temp. 26.0 C / 299.1 K
Sample #6, Operator: aherrmann
VMDR5-600 "varianproco"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.000 sec
Width 113.6 kHz
16 repetitions
OBSERVE F19, 564.3312865 MHz
DATA PROCESSING
Line broadening 0.9 Hz
FT size 262144
Total time 0 min 36 sec



ls-2-91-3-2

File: nmr600/Zakarian/lsmith/vnmrsys/data/ls-2-91-3-2.fid

Pulse Sequence: s2pul

Solvent: cdcl3

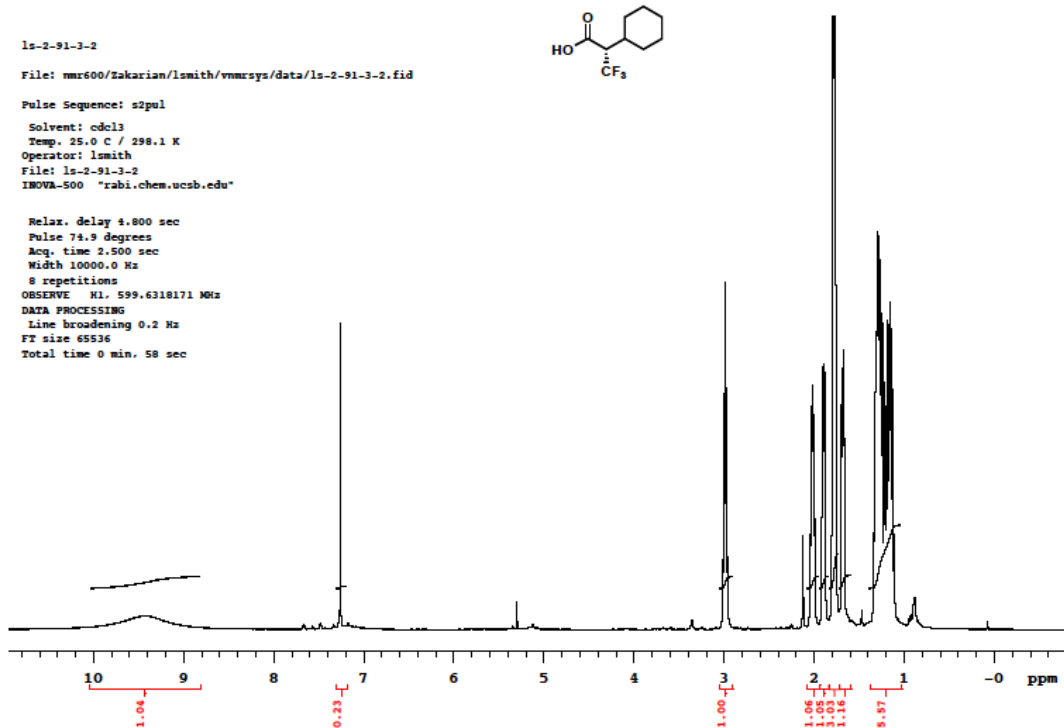
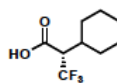
Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-2-91-3-2

INOVA-500 "rabi.chem.ucsb.edu"

Relax. delay 1.000 sec
Pulse 74.9 degrees
Acq. time 2.500 sec
Width 10000.0 Hz
8 repetitions
OBSERVE H1, 599.6318171 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FF size 65536
Total time 0 min. 58 sec



ls-2-91-3-2-carbon

File: nmr600/Zakarian/lsmith/vnmrsys/data/ls-2-91-3-2-carbon.fid

Pulse Sequence: s2pul

Solvent: cdcl3

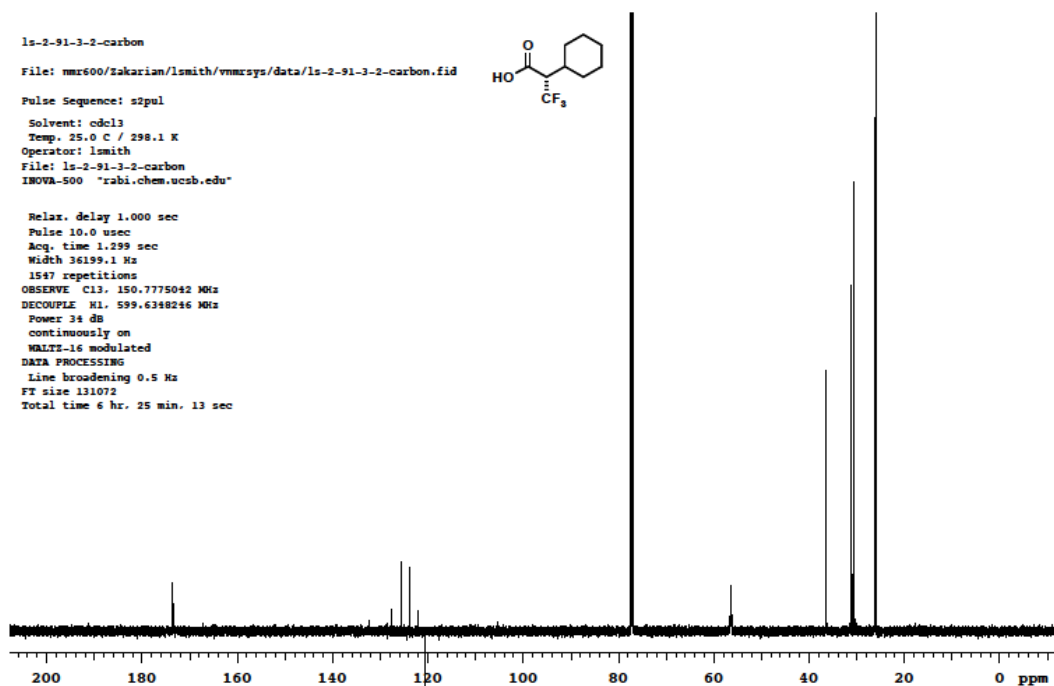
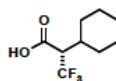
Temp. 25.0 C / 298.1 K

Operator: lsmith

File: ls-2-91-3-2-carbon

INOVA-500 "rabi.chem.ucsb.edu"

Relax. delay 1.000 sec
Pulse 10.0 usec
Acq. time 1.299 sec
Width 36199.1 Hz
1547 repetitions
OBSERVE C13, 150.7775042 MHz
DECOUPLE H1, 599.6348246 MHz
Power 34 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr. 25 min. 13 sec



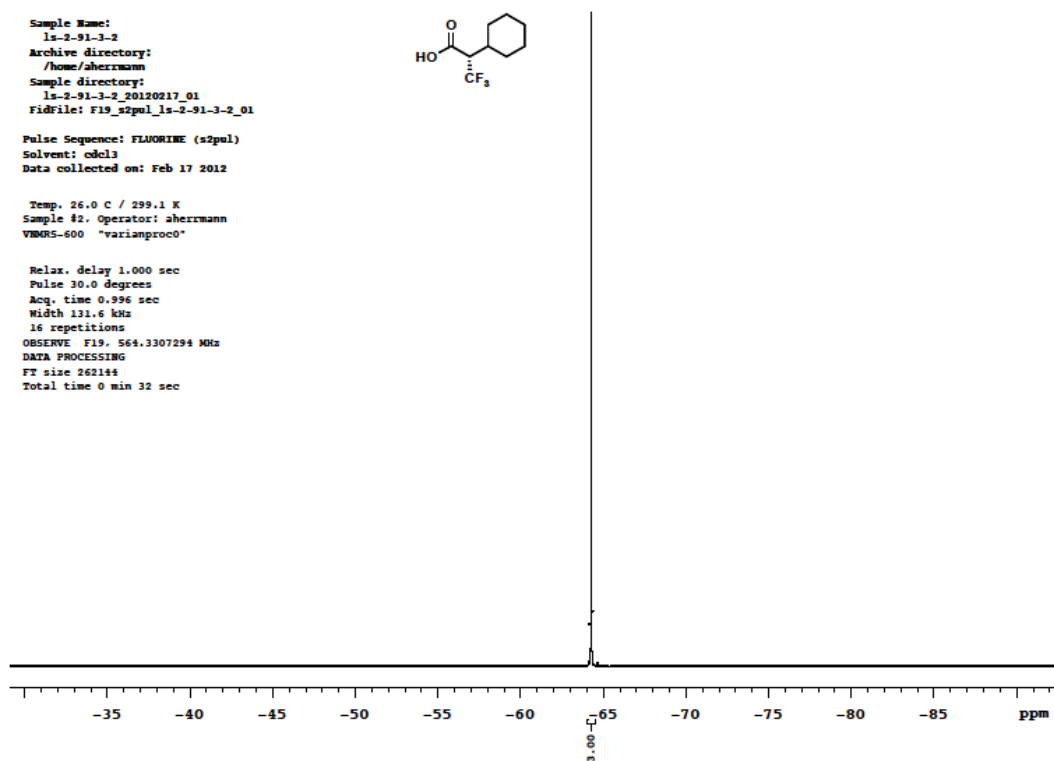
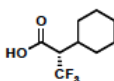
19F
600MHz

Sample Name:
ls-2-91-3-2
Archive directory:
/home/aherrmann
Sample directory:
ls-2-91-3-2_20120217_01
FidFile: F19_s2pul_ls-2-91-3-2_01

Pulse Sequence: FLUORINE (s2pul)
Solvent: cdcl3
Data collected on: Feb 17 2012

Temp. 26.0 C / 299.1 K
Sample #2. Operator: aherrmann
VNS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 0.996 sec
Width 131.6 kHz
16 repetitions
OBSERVE F19. 564.3307294 MHz
DATA PROCESSING
FT size 262144
Total time 0 min 32 sec



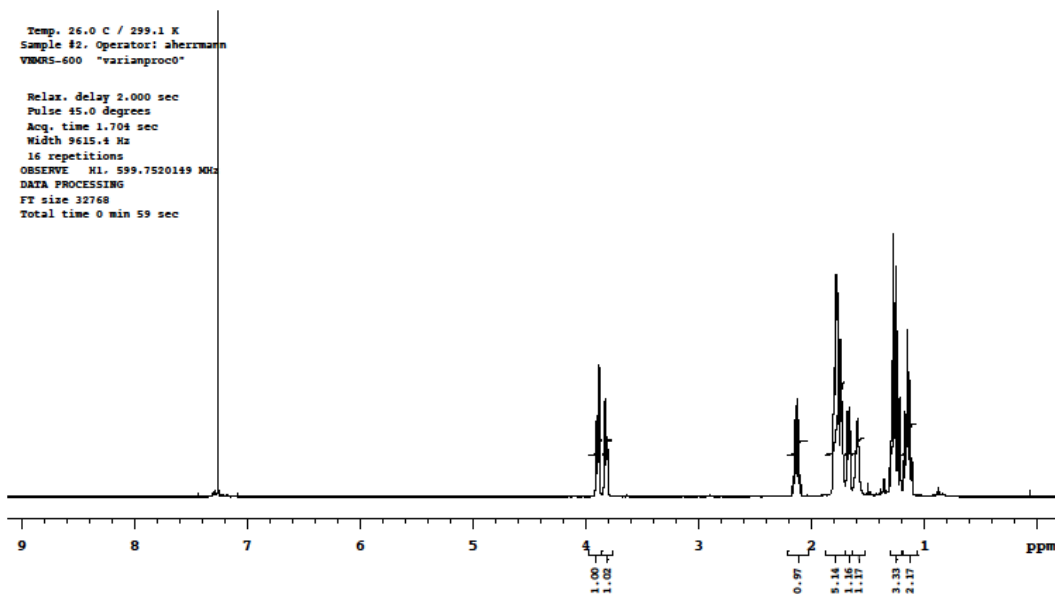
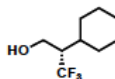
600MHz (H₂O)

Sample Name:
ath-3-295-a
Archive directory:
/home/aherrmann
Sample directory:
ath-3-295-a_20120218_01
FidFile: H1_s2pul_ath-3-295-a_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 18 2012

Temp. 26.0 C / 299.1 K
Sample #2, Operator: aherrmann
VMDR5-600 "varianproc0"

Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 9615.4 Hz
16 repetitions
OBSERVE H1, 599.7520149 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 59 sec

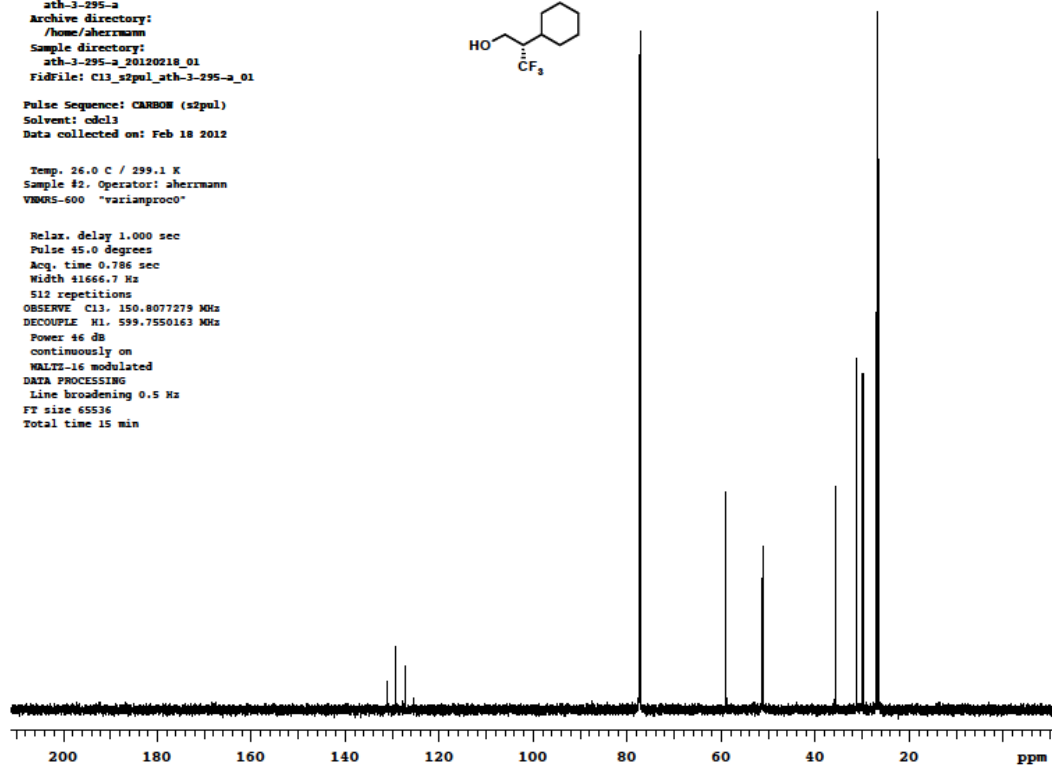
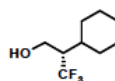


Sample Name:
ath-3-295-a
Archive directory:
/home/aherrmann
Sample directory:
ath-3-295-a_20120218_01
FidFile: C13_s2pul_ath-3-295-a_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 18 2012

Temp. 26.0 C / 299.1 K
Sample #2, Operator: aherrmann
VMDR5-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.786 sec
Width 41666.7 Hz
512 repetitions
OBSERVE C13, 150.8077279 MHz
DECOUPLE H1, 599.7550163 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 15 min



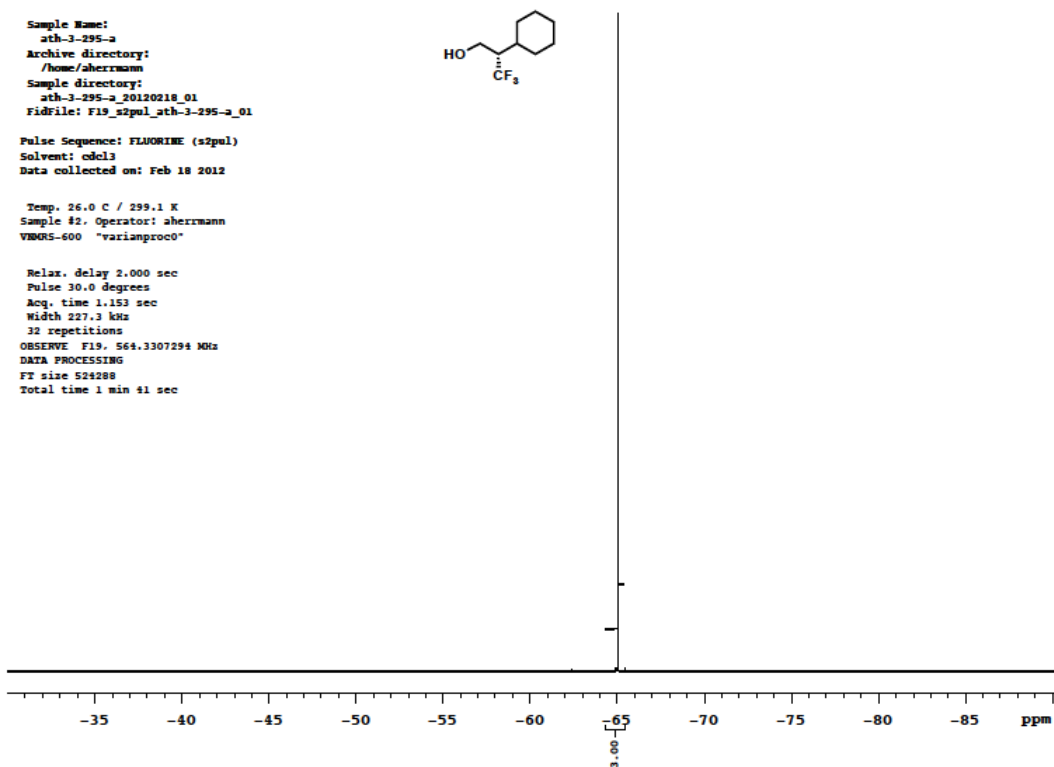
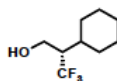
600MHz (MUL)

Sample Name:
ath-3-295-a
Archive directory:
/home/aherrmann
Sample directory:
ath-3-295-a_20120218_01
FidFile: F19_s2pul_ath-3-295-a_01

Pulse Sequence: FLUORINE (s2pul)
Solvent: cdcl3
Data collected on: Feb 18 2012

Temp. 26.0 C / 299.1 K
Sample #: Operator: aherrmann
VMDGS-600 "varianproc0"

Relax. delay 2.000 sec
Pulse 30.0 degrees
Acq. time 1.153 sec
Width 227.3 kHz
32 repetitions
OBSERVE F19, 564.3307294 MHz
DATA PROCESSING
FT size 524288
Total time 1 min 41 sec

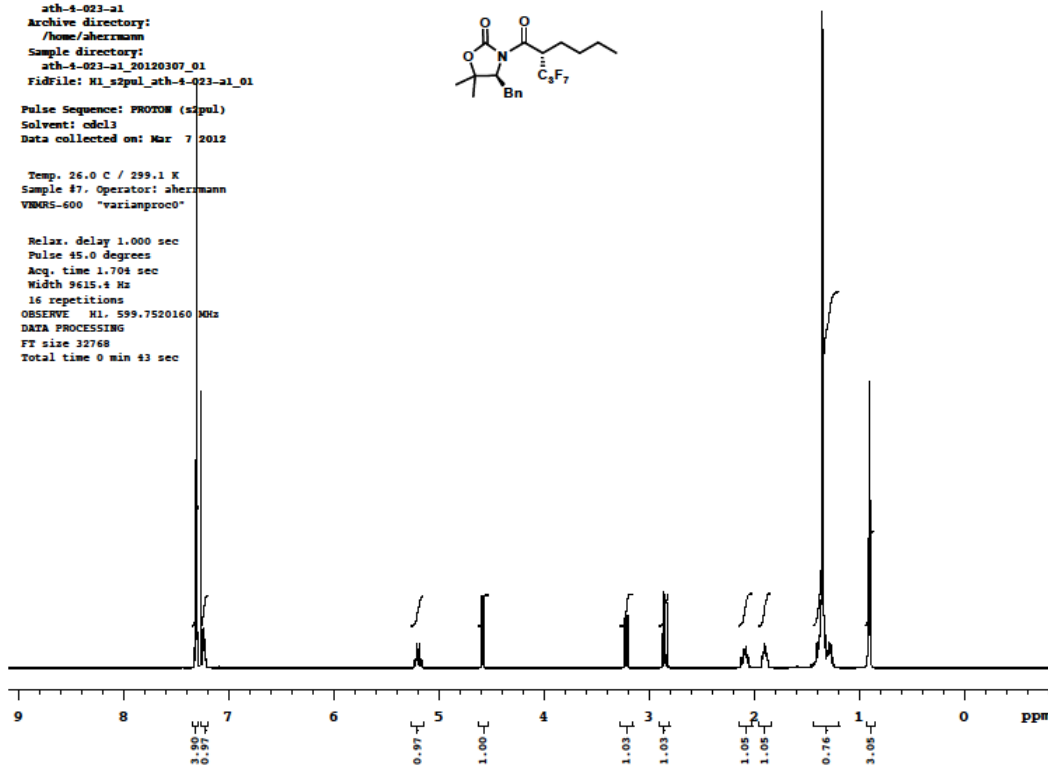
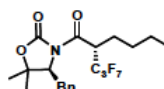


Sample Name:
ath-4-023-a1
Archive directory:
/home/aherrmann
Sample directory:
ath-4-023-a1_20120307_01
FidFile: M1_s2pul_ath-4-023-a1_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 7 2012

Temp. 26.0 C / 299.1 K
Sample #7, Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 9615.4 Hz
16 repetitions
OBSERVE M1. 599.7520160 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 43 sec

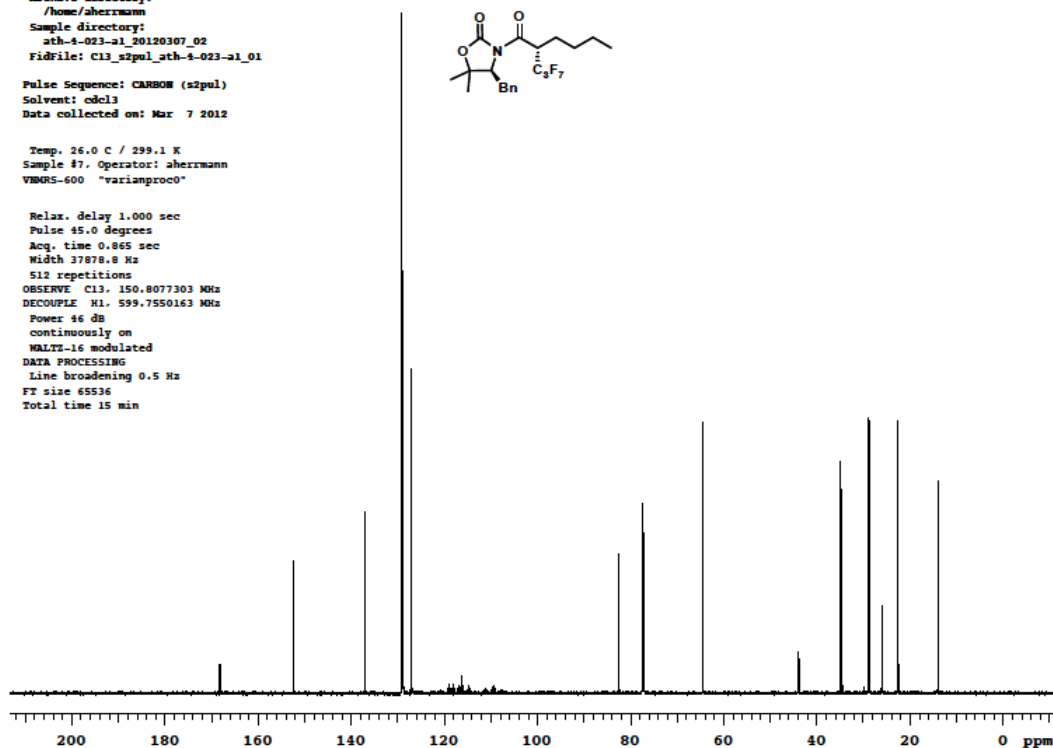
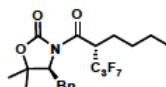


Sample Name:
ath-4-023-a1
Archive directory:
/home/aherrmann
Sample directory:
ath-4-023-a1_20120307_02
FidFile: C13_s2pul_ath-4-023-a1_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 7 2012

Temp. 26.0 C / 299.1 K
Sample #7, Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.865 sec
Width 37878.8 Hz
512 repetitions
OBSERVE C13. 150.8077303 MHz
DECOUPLE M1. 599.7550163 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 15 min

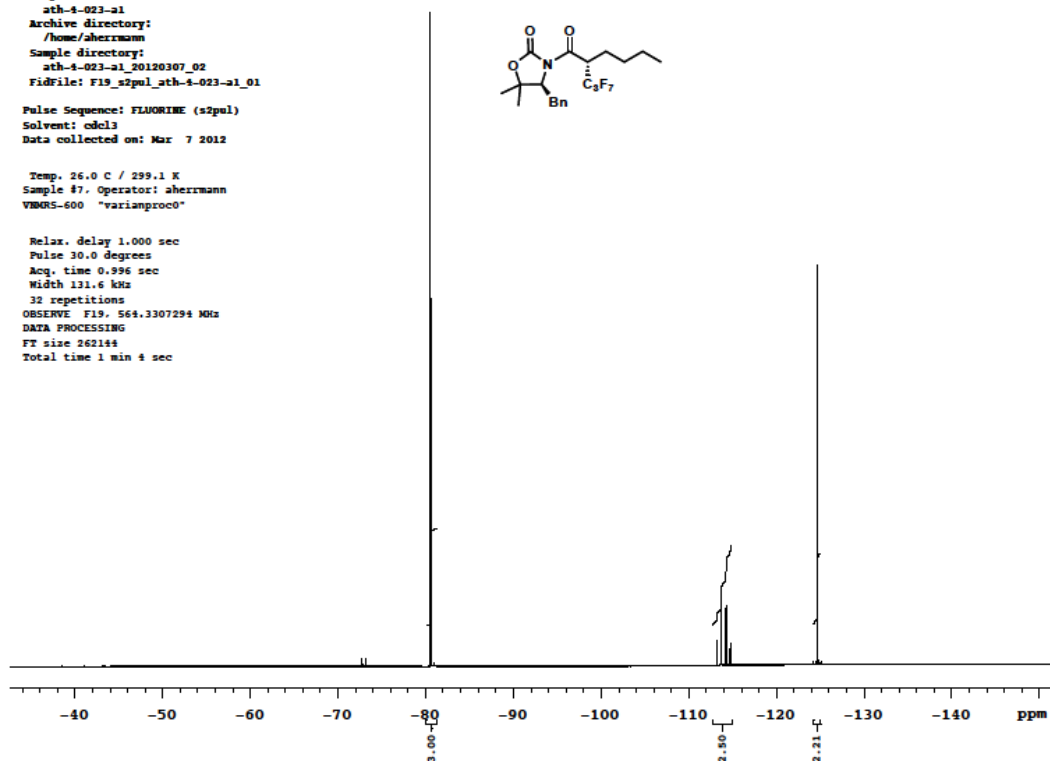
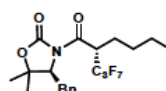


Sample Name:
 ath-4-023-a1
 Archive directory:
 /home/aherrmann
 Sample directory:
 ath-4-023-a1_20120307_02
 FidFile: F19_s2pul_ath-4-023-a1_01

Pulse Sequence: FLUORINE (s2pul)
 Solvent: cdcl3
 Data collected on: Mar 7 2012

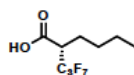
Temp. 26.0 C / 299.1 K
 Sample #7, Operator: aherrmann
 VMDIS-600 "varianproc0"

Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 0.996 sec
 Width 131.6 kHz
 32 repetitions
 OBSERVE F19, 564.3307294 MHz
 DATA PROCESSING
 FT size 262144
 Total time 1 min 4 sec



600MHz

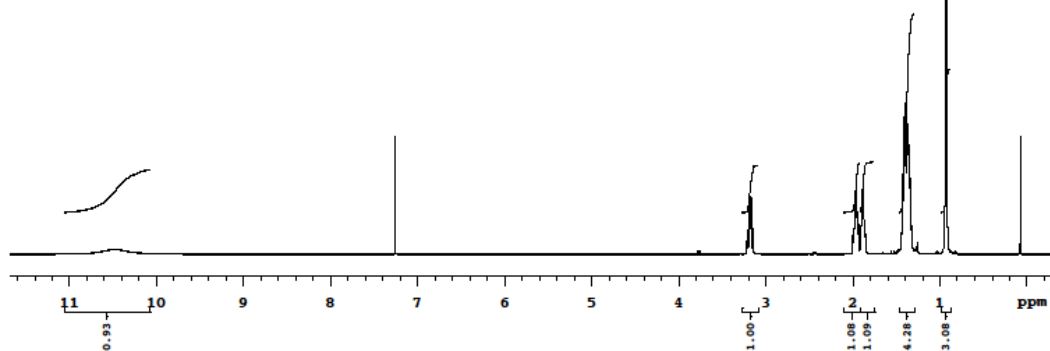
Sample Name:
ath-4-028-acid
Archive directory:
/home/aherrmann
Sample directory:
ath-4-028-acid_20120312_01
Fidfile: M1_s2pul_ath-4-028-acid_01



Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 12 2012

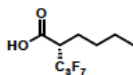
Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VIBRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 9615.4 Hz
64 repetitions
OBSERVE M1, 599.7520160 MHz
DATA PROCESSING
FT size 32768
Total time 2 min 53 sec



600MHz

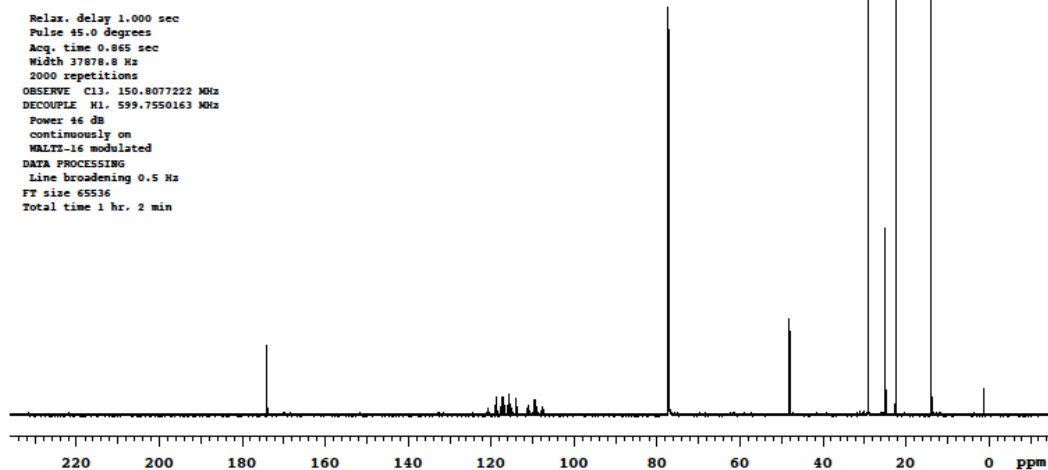
Sample Name:
ath-4-028-acid
Archive directory:
/home/aherrmann
Sample directory:
ath-4-028-acid_20120312_01
Fidfile: C13_s2pul_ath-4-028-acid_01



Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 12 2012

Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VIBRS-600 "varianproc0"

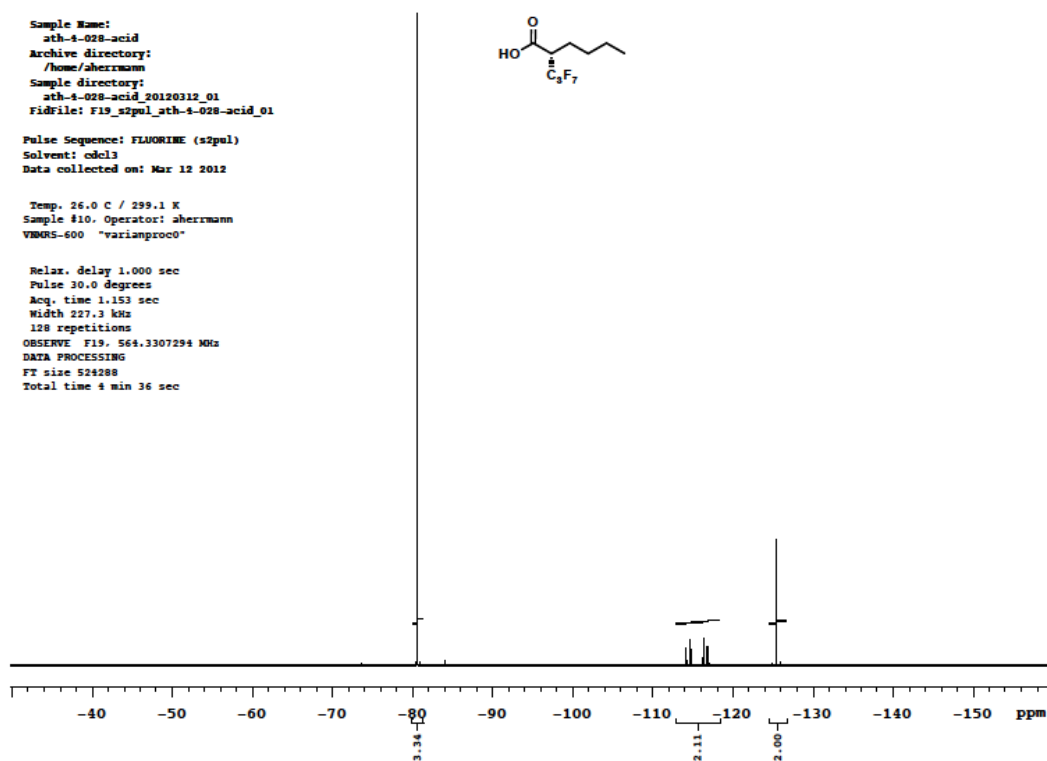
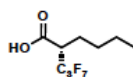
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.065 sec
Width 37879.8 Hz
2000 repetitions
OBSERVE C13, 150.8077222 MHz
DECOUPLE M1, 599.7550163 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 2 min



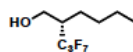
```
Sample Name:
ath-4-028-acid
Archive directory:
/home/aherrmann
Sample directory:
ath-4-028-acid_20120312_01
FidFile: F19_s2pul_ath-4-028-acid_01
```

Temp. 26.0 C / 299.1 K
Sample #10, Operator: aherrmann
VIMS-600 "varianproc0"

```
Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 1.153 sec
Width 227.3 kHz
128 repetitions
OBSERVE F19, 564.3307294 MHz
DATA PROCESSING
FT size 524288
Total time 4 min 36 sec
```



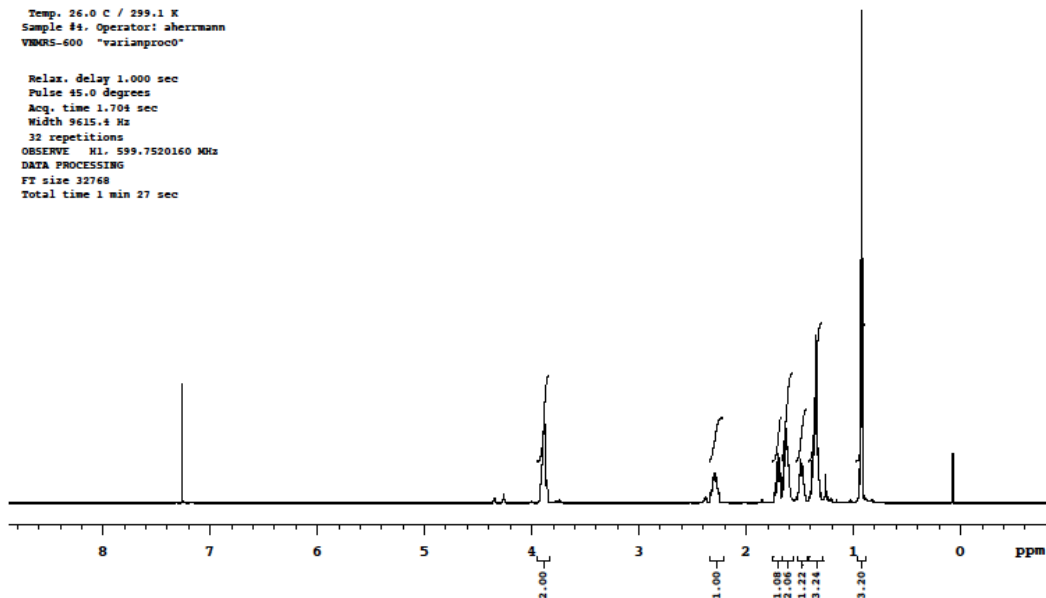
Sample Name:
ath-4-024-a3
Archive directory:
/home/aherrmann
Sample directory:
ath-4-024-a3_20120309_01
Fidfile: H1_s2pul_ath-4-024-a3_01



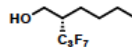
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 9 2012

Temp. 26.0 C / 299.1 K
Sample #4. Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 9615.4 Hz
32 repetitions
OBSERVE H1, 599.7520160 MHz
DATA PROCESSING
FT size 32768
Total time 1 min 27 sec



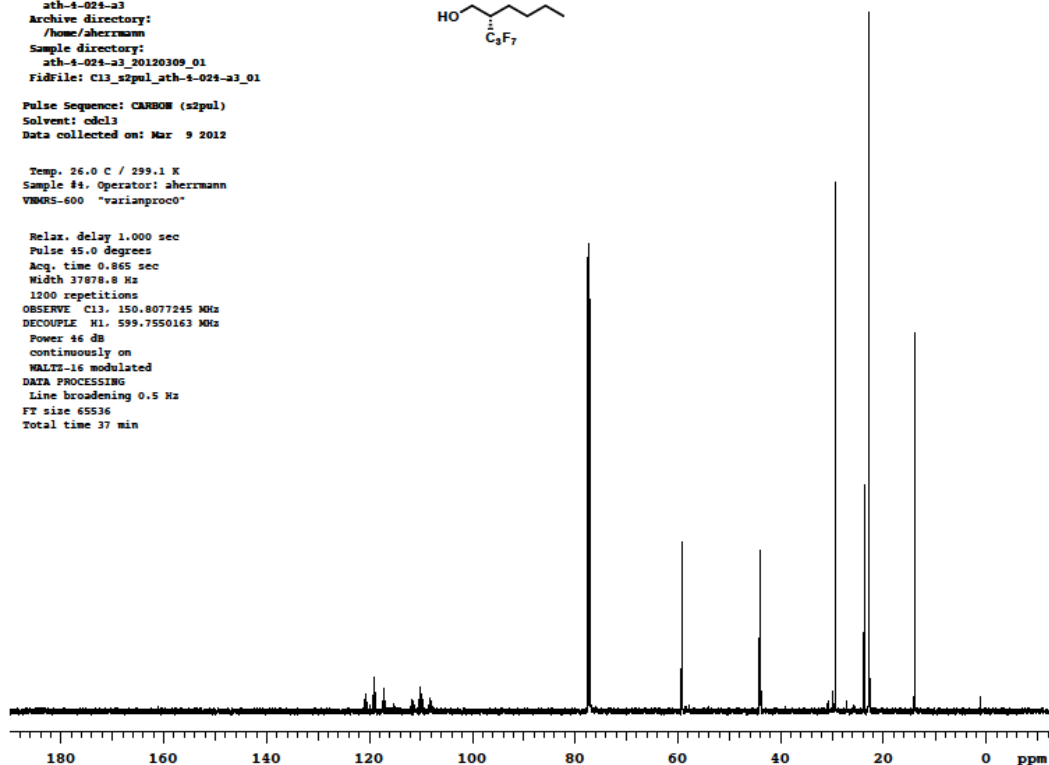
Sample Name:
ath-4-024-a3
Archive directory:
/home/aherrmann
Sample directory:
ath-4-024-a3_20120309_01
Fidfile: C13_s2pul_ath-4-024-a3_01



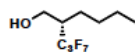
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Mar 9 2012

Temp. 26.0 C / 299.1 K
Sample #4. Operator: aherrmann
VNMRS-600 "varianproc0"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 0.865 sec
Width 37878.8 Hz
1200 repetitions
OBSERVE C13, 150.8077245 MHz
DECOUPLE H1, 599.7550163 MHz
Power 46 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 37 min



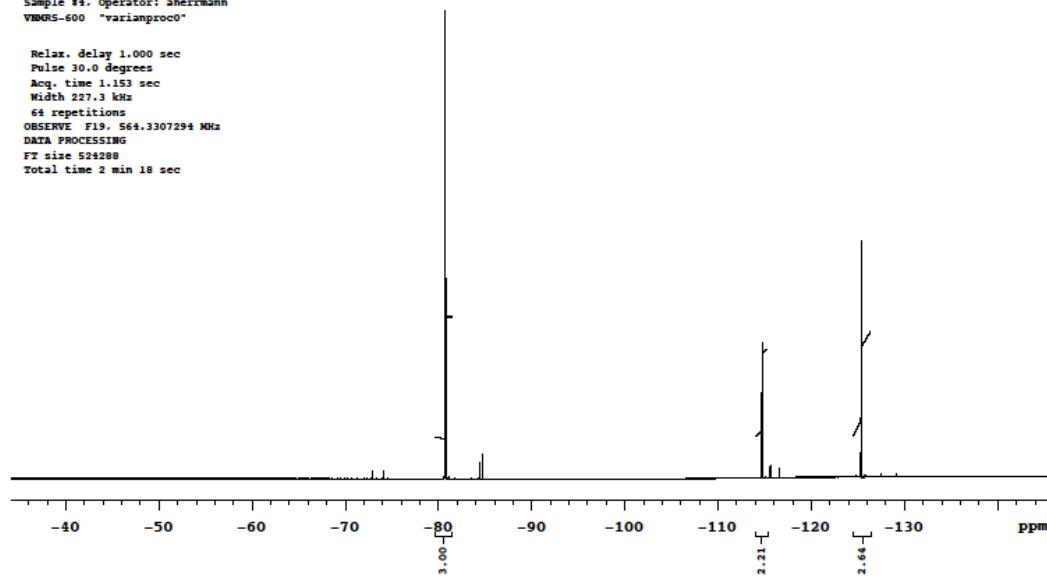
Sample Name:
 ath-4-024-a3
 Archive directory:
 /home/sherrmann
 Sample directory:
 ath-4-024-a3_20120309_01
 Fidfile: F19_s2pul_ath-4-024-a3_01



Pulse Sequence: FLUORINE (s2pul)
 Solvent: cdcl3
 Data collected on: Mar 9 2012

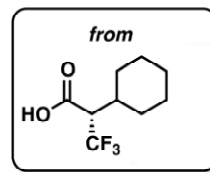
Temp. 26.0 C / 299.1 K
 Sample #4. Operator: sherrmann
 VMDR5-600 "varianproc0"

Relax. delay 1.000 sec
 Pulse 30.0 degrees
 Acq. time 1.153 sec
 Width 227.3 kHz
 64 repetitions
 OBSERVE F19: 564.3307294 MHz
 DATA PROCESSING
 FT size 524288
 Total time 2 min 18 sec

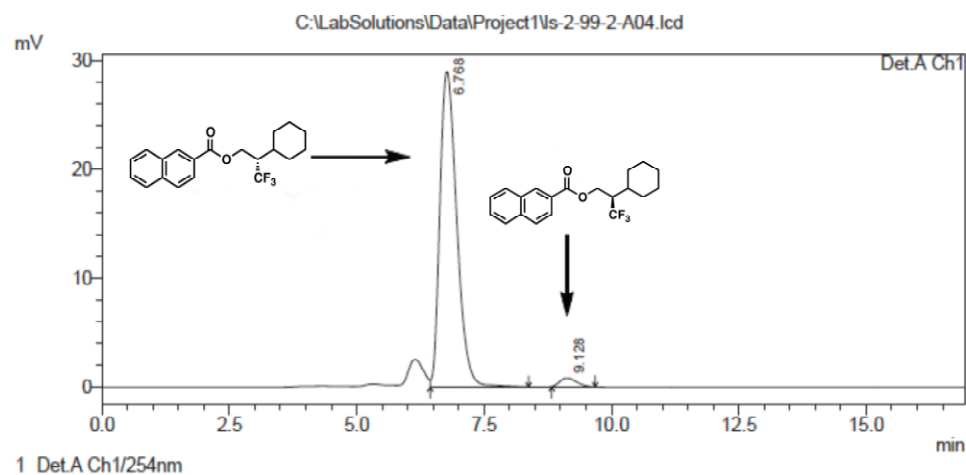


==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\Is-2-99-2-A04.lcd
 Acquired by : Admin
 Sample Name : Is-2-99-2-A
 Sample ID : Is-2-99-2-A
 Vial # :
 Injection Volume : 50 uL
 Data File Name : Is-2-99-2-A04.lcd
 Method File Name : ath-OD-H-analytical 0.46cm x 25cm.lcm
 Batch File Name :
 Report File Name : Default.lcr
 Data Acquired : 3/14/2012 12:33:48 AM
 Data Processed : 3/14/2012 12:50:44 AM



<Chromatogram>



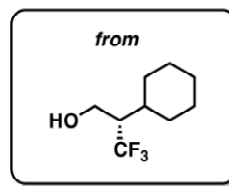
Detector A Ch1 254nm

PeakTable

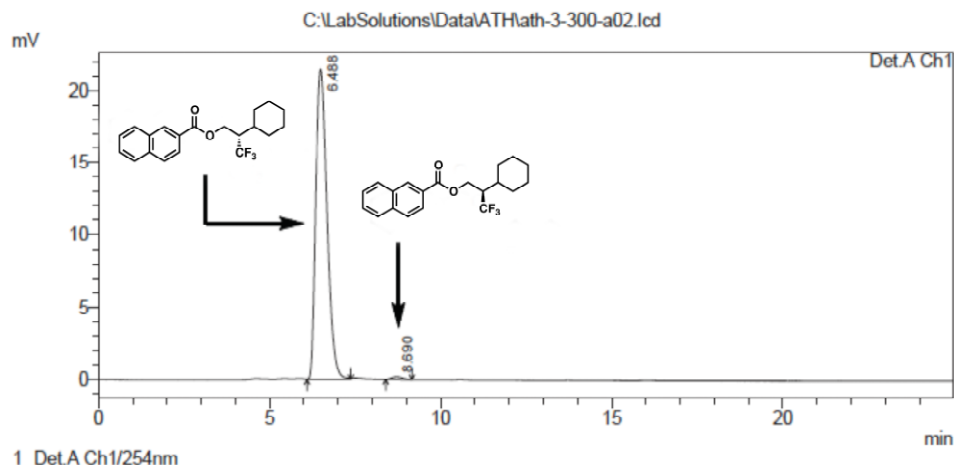
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.768	668339	28968	97.217	97.207
2	9.128	19130	832	2.783	2.793
Total		687468	29800	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

Acquired by : Admin
Sample Name : ath-3-300-a
Sample ID : ath-3-300-a
Vial # :
Injection Volume : 50 uL
Data File Name : ath-3-300-a02.lcd
Method File Name : ath-OD-H-analytical 0.46cm x 25cm.lcm
Batch File Name :
Report File Name : Default.lcr
Data Acquired : 2/27/2012 3:59:07 PM
Data Processed : 2/27/2012 4:24:06 PM



<Chromatogram>

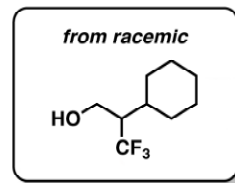


PeakTable

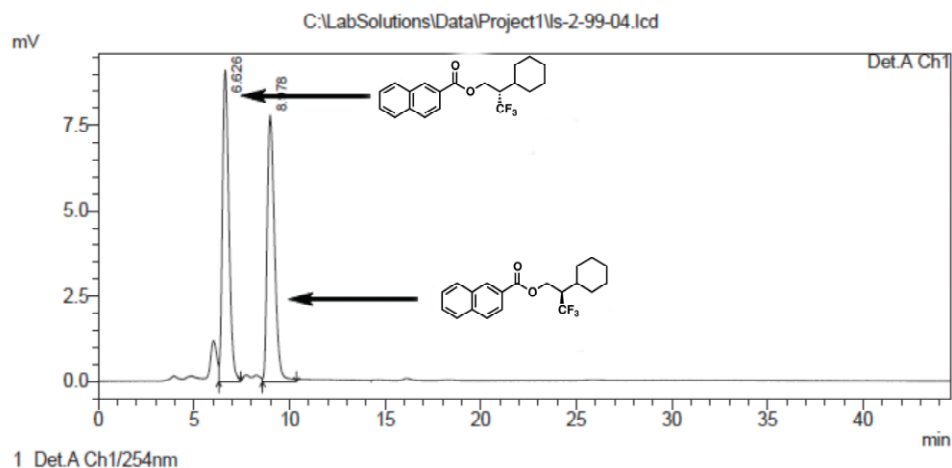
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.488	491241	21496	99.200	99.165
2	8.690	3960	181	0.800	0.835
Total		495202	21677	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

Acquired by : Admin
 Sample Name : ath-4-011-a1
 Sample ID : ath-4-011-a1
 Vial # :
 Injection Volume : 50 uL
 Data File Name : ls-2-99-04.lcd
 Method File Name : ath-OD-H-analytical 0.46cm x 25cm.lcm
 Batch File Name :
 Report File Name : Default.lcr
 Data Acquired : 2/29/2012 1:59:39 PM
 Data Processed : 2/29/2012 2:44:14 PM



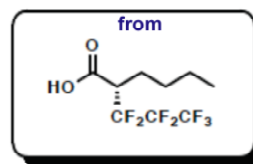
<Chromatogram>



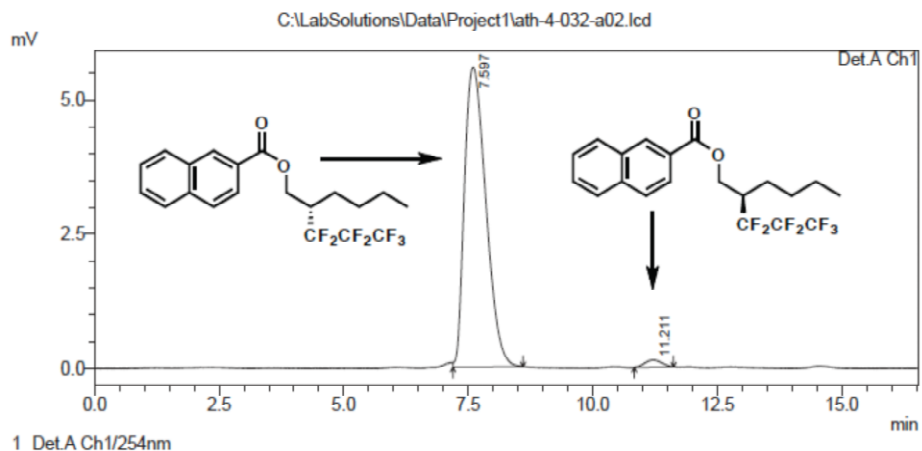
PeakTable					
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.626	216113	9135	50.485	53.946
2	8.978	211957	7798	49.515	46.054
Total		428070	16933	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

Acquired by : Admin
 Sample Name : ath-4-032-a
 Sample ID : ath-4-032-a
 Vial # :
 Injection Volume : 20 uL
 Data File Name : ath-4-032-a02.lcd
 Method File Name : ath-OD-H-analytical 0.46cm x 25cm.lcm
 Batch File Name :
 Report File Name : Default.lcr
 Data Acquired : 3/15/2012 1:45:41 AM
 Data Processed : 3/15/2012 2:02:14 AM



<Chromatogram>

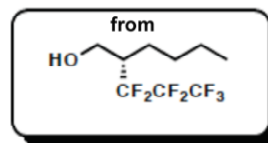


PeakTable

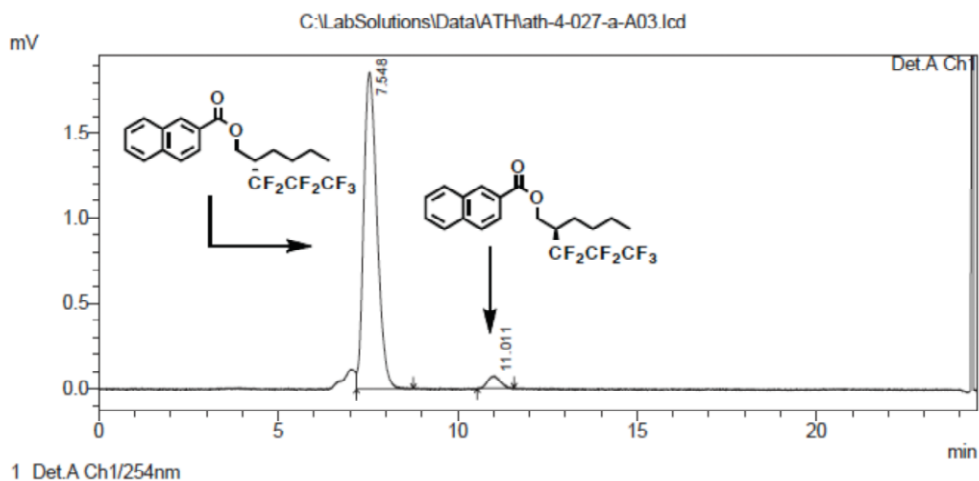
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.597	166730	5591	98.124	97.667
2	11.211	3188	134	1.876	2.333
Total		169918	5724	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\ATH\ath-4-027-a-A03.lcd
 Acquired by : Admin
 Sample Name : ath-4-027-a-A
 Sample ID : ath-4-027-a-A
 Vial # :
 Injection Volume : 5 uL
 Data File Name : ath-4-027-a-A03.lcd
 Method File Name : ath-OD-H-analytical 0.46cm x 25cm.lcm
 Batch File Name :
 Report File Name : Default.lcr
 Data Acquired : 3/13/2012 2:20:14 PM
 Data Processed : 3/13/2012 2:44:43 PM



<Chromatogram>



PeakTable

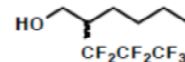
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.548	47647	1859	96.625	96.392
2	11.011	1664	70	3.375	3.608
Total		49311	1929	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\Data\Project1\Is-2-109-04.lcd

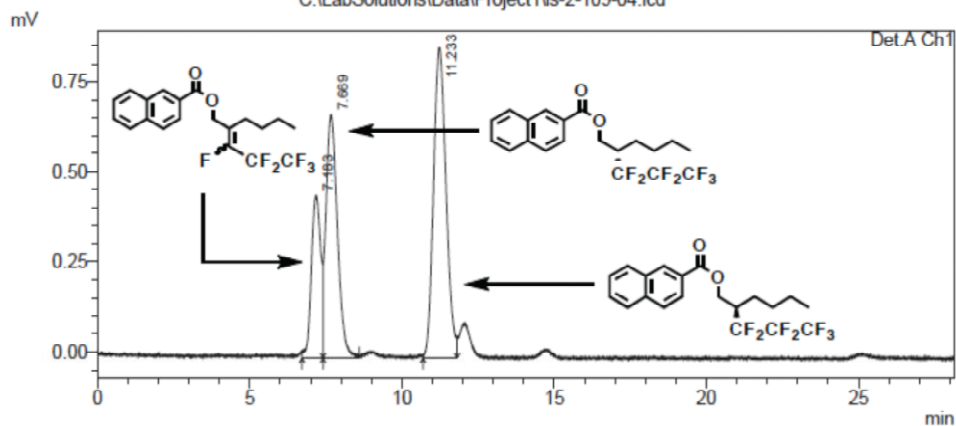
Acquired by : Admin
 Sample Name : Is-2-109-3
 Sample ID : Is-2-109-3
 Vial # :
 Injection Volume : 10 uL
 Data File Name : Is-2-109-04.lcd
 Method File Name : ath-OD-H-analytical 0.46cm x 25cm.lcm
 Batch File Name :
 Report File Name : Default.lcr
 Data Acquired : 3/15/2012 12:32:24 AM
 Data Processed : 3/15/2012 1:00:32 AM

from racemic



<Chromatogram>

C:\LabSolutions\Data\Project1\Is-2-109-04.lcd



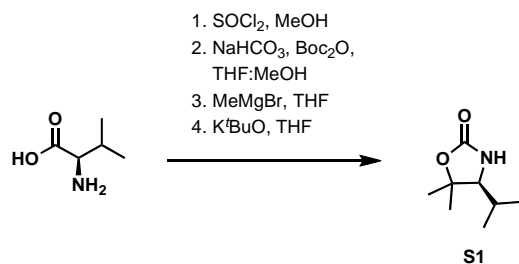
1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.183	9631	452	18.533	22.731
2	7.669	17653	677	33.972	34.035
3	11.233	24680	860	47.495	43.234
Total		51964	1989	100.000	100.000

3-8: α -Fluorination of *N*-Acyl Oxazolidinones Supporting Information



(S)-4-Isopropyl-5,5-dimethyloxazolidin-2-one (S2). Thionyl chloride (31.1 mL, 427 mmol) was added dropwise to a solution of L-valine (25.0 g, 213 mmol) in methanol (430 mL) at 0 °C. The reaction was stirred for 10 min at 0 °C, and then heated to reflux for 4 h. The solution was cooled to rt and methanol was removed in vacuo. The crude residue was submitted to the next step without purification.

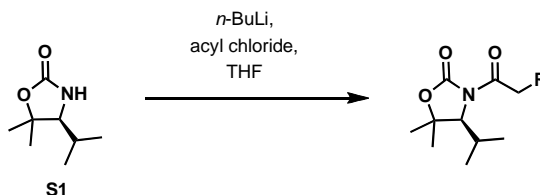
Sodium hydrogen carbonate (53.7 g, 640 mmol) was added to a solution of crude substrate (213 mmol) in a 4:1 mixture of THF:MeOH (560 mL) at 0 °C and stirred for 5 min. Di-tert-butyl dicarbonate (47.0 g, 215 mmol) was added to the mixture at 0 °C. The reaction was warmed to rt and stirred for 2 h and then quenched with water. The layers were separated. The aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic layers were washed with saturated sodium bicarbonate, brine, and dried with sodium sulfate and concentrated *in vacuo* to afford a yellow oil. The crude residue was submitted to the next step without further purification.

Methylmagnesium bromide (3.0 M in Et_2O , 250 mL, 750 mmol) was added dropwise to a solution of the crude substrate (213 mmol) in THF (500 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min, then warmed to rt and stirred for 48 h. The solution was cooled to 0 °C and quenched with saturated ammonium chloride. The layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic

layers were washed with brine and dried with sodium sulfate and concentrated *in vacuo* delivering a light yellow oil. The crude residue was submitted to the next step without further purification.

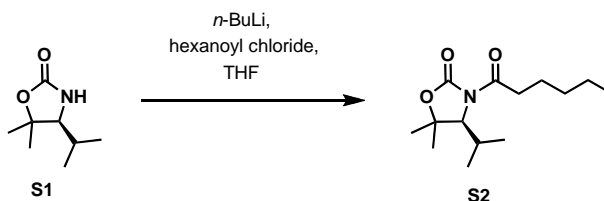
Potassium tert-butoxide (26.8 g, 239 mmol) was added to a solution of the crude substrate (213 mmol) in THF (575 mL) at 0 °C. The reaction was warmed to rt and stirred for 2.5 h. The reaction was then quenched with saturated aqueous ammonium chloride. The layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The crude product was purified by column chromatography (silica, 40% ethyl acetate in hexanes, 75% ethyl acetate in hexanes) to afford the white/yellow solid oxazolidinone **S2** (28.1 g, 179 mmol, 84%).

Standard procedure 1: Synthesis of *N*-acyl oxazolidinones via acyl chloride

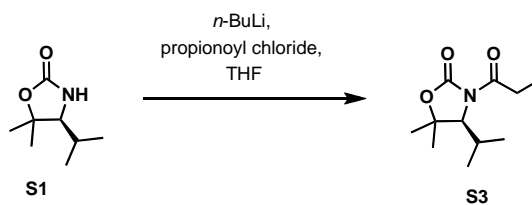


n-Butyllithium (2.48 M in hexanes, 2.88 ml, 7.14 mmol, 1.1 equiv) was added to a solution of **S2** (1.02 g, 6.49 mmol, 1.0 equiv) in tetrahydrofuran (22.0 ml, 0.30 M) at -78°C and stirred at room temperature for 30 minutes. The solution was cooled to -78°C and the corresponding acyl chloride (7.78 mmol, 1.2 equiv) was added to the reaction mixture and stirred for 15 min at -78°C . The reaction solution was warmed to rt and stirred for 2 h. The reaction was quenched with saturated ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 20 ml). The combined organic layers

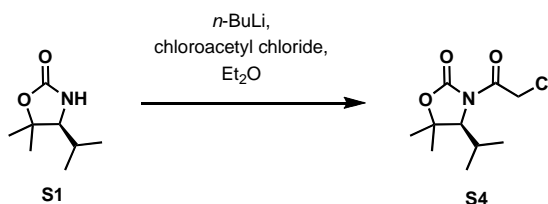
were washed with brine, dried over sodium sulfate, concentrated *in vacuo*, and purified by column chromatography to give the corresponding *N*-acyl oxazolidinone.



(S)-3-Hexanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.49). The title compound was prepared from commercially available hexanoyl chloride (1.08 ml, 7.78 mmol) following standard procedure 1 for the synthesis of *N*-acyl oxazolidinones via acyl chloride and was obtained as a yellow oil (1.36 g, 5.32 mmol, 82%) after purification by column chromatography (silica, 6% ethyl acetate in hexanes – 12% ethyl acetate in hexanes). $\alpha_D^{27} + 31.21$ (*c* 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃); δ (ppm): 4.11 (d, *J* = 3.3 Hz, 1H), 3.01 – 2.92 (m, 1H), 2.87 – 2.79 (m, 1H), 2.15 – 2.06 (m, 1H), 1.69 – 1.59 (m, 2H), 1.47 (s, 3H), 1.34 (s, 3H), 1.33 – 1.29 (m, 4H), 0.99 (dd, *J* = 7.0, 3.5 Hz, 3H), 0.91 (dd, *J* = 6.8, 3.5 Hz, 3H), 0.88 – 0.84 (m, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 173.84 (s), 153.46 (s), 82.56 (s), 66.12 (s), 35.34 (s), 31.23 (s), 29.46 (s), 28.72 (s), 24.34 (s), 22.31 (s), 21.41 (s), 21.30 (s), 16.97 (s), 13.83 (s); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₄H₂₅NO₃Na, 278.1732; found, 278.1728.

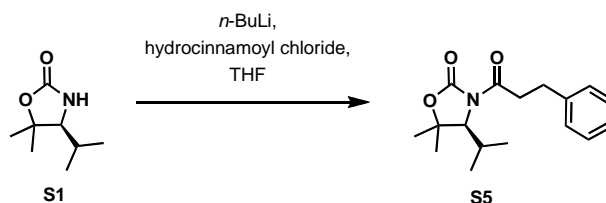


(S)-4-Isopropyl-5,5-dimethyl-3-propionyloxazolidin-2-one (3.50). The title compound was prepared from commercially available propionoyl chloride (0.68 mL, 7.78 mmol) following standard procedure 1 for the synthesis of *N*-acyl oxazolidinones via acyl chloride and was obtained as a white solid (1.22 g, 5.72 mmol, 88%) after purification by column chromatography (silica, 10 ethyl acetate in hexanes - 15% ethyl acetate in hexanes). $\alpha_D^{25} + 38.28$ (*c* 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 4.13 (d, $J = 3.3$ Hz, 1H), 2.99 (dddd, $J = 17.4, 7.4$ Hz, 1H), 2.89 (dddd, $J = 17.4, 7.3$ Hz, 1H), 2.13 (ddd, $J = 13.8, 6.9, 3.4$ Hz, 1H), 1.49 (s, 3H), 1.36 (s, 3H), 1.17 (dd, $J = 9.6, 5.2$ Hz, 3H), 1.01 (d, $J = 7.0$ Hz, 3H), 0.93 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 174.59 (s), 153.56 (s), 82.71 (s), 66.24 (s), 29.51 (s), 29.07 (s), 28.80 (s), 21.43 (s), 21.37 (s), 17.02 (s), 8.72 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{19}\text{NO}_3\text{Na}$, 236.1263; found, 236.1268.



(S)-3-(2-Chloroacetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.51). The title compound was prepared from commercially available chloroacetyl chloride (0.62 mL, 7.78 mmol) following standard procedure 1 for the synthesis of *N*-acyl oxazolidinones via acyl chloride using diethyl ether (22.0 mL, 0.30 M) and was obtained as a yellow oil (1.25 g, 5.38

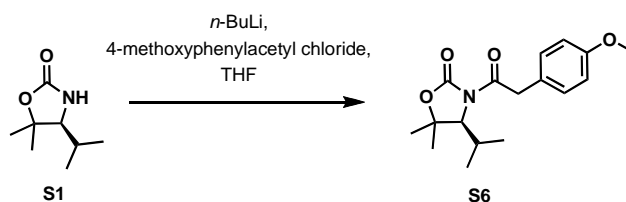
mmol, 83%) after purification by column chromatography (silica, 10 ethyl acetate in hexanes - 15% ethyl acetate in hexanes). $\alpha_D^{27} + 39.55$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); δ (ppm): 4.75 (ddd, $J = 15.3$ Hz, 2H), 4.16 (d, $J = 3.2$ Hz, 1H), 2.22 – 2.14 (m, 1H), 1.54 (s, 3H), 1.42 (s, 3H), 1.06 (d, $J = 7.0$ Hz, 3H), 0.97 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); δ (ppm): 166.44 (s), 152.97 (s), 83.96 (s), 66.77 (s), 43.38 (s), 29.37 (s), 28.63 (s), 21.29 (s), 21.18 (s), 16.67 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{10}\text{H}_{16}\text{ClNO}_3\text{Na}$, 256.0716; found, 256.0700.



(S)-4-Isopropyl-5,5-dimethyl-3-(3-phenylpropanoyl)oxazolidin-2-one (3.52). The title compound was prepared from commercially available hydrocinnamoyl chloride (1.16 mL, 7.78 mmol) following standard procedure 1 for the synthesis of N-acyl oxazolidinones via acyl chloride and was obtained as a yellow oil (1.41 g, 4.87 mmol, 74%) after purification by column chromatography (silica, 10 ethyl acetate in hexanes - 18% ethyl acetate in hexanes). $\alpha_D^{27} + 36.16$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.30 – 7.26 (m, 3H), 7.25 (s, 1H), 7.21 – 7.17 (m, 1H), 4.13 (d, $J = 3.3$ Hz, 1H), 3.34 (ddd, $J = 16.5, 9.0, 6.3$ Hz, 1H), 3.29 – 3.22 (m, 1H), 3.08 – 2.93 (m, 2H), 2.12 (dddd, $J = 13.8, 6.9, 3.5$ Hz, 1H), 1.50 (s, 3H), 1.32 (s, 3H), 0.99 (d, $J = 7.0$ Hz, 3H), 0.91 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); δ (ppm): 172.89 (s), 153.48 (s), 140.41 (s), 128.46 (s), 128.39 (s),

126.15 (s), 82.77 (s), 66.27 (s), 36.82 (s), 30.68 (s), 29.47 (s), 28.70 (s), 21.35 (s), 16.99 (s);

HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{17}H_{23}NO_3Na$, 312.1576; found, 312.1559.



(S)-4-Isopropyl-3-(2-(4-methoxyphenyl)acetyl)-5,5-dimethyloxazolidin-2-one (3.53).

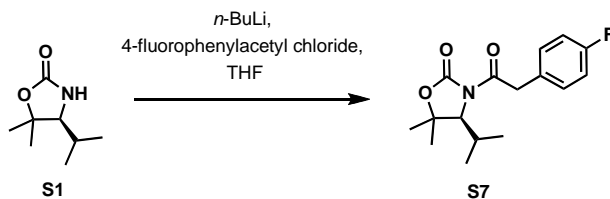
The title compound was prepared from commercially available 4-methoxyphenylacetyl chloride (1.19 mL, 7.78 mmol) following standard procedure 1 for the synthesis of N-acyl oxazolidinones via acyl chloride and was obtained as a yellow oil (1.02 g, 3.34 mmol, 52%)

after purification by column chromatography (silica, 15 - 22% ethyl acetate in hexanes. α_D^{26}

70.63 (c 1.0, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.27 (s, 1H), 7.26 – 7.25 (m, 1H), 6.85 (d, J = 8.6 Hz, 2H), 4.30 (d, J = 15.0 Hz, 1H), 4.19 (d, J = 15.0 Hz, 1H), 4.12 (d, J = 3.1 Hz, 1H), 3.79 (s, 3H), 2.10 (ddd, J = 10.5, 6.8, 3.4 Hz, 1H), 1.49 (s, 3H), 1.31 (s, 3H),

0.95 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 172.05 (s), 158.62 (s), 153.48 (s), 130.60 (s), 125.97 (s), 113.86 (s), 82.77 (s), 66.39 (s), 55.14 (s), 40.58 (s), 29.53 (s), 28.69 (s), 21.38 (s), 21.29 (s), 16.79 (s); HRMS-EI (m/z):

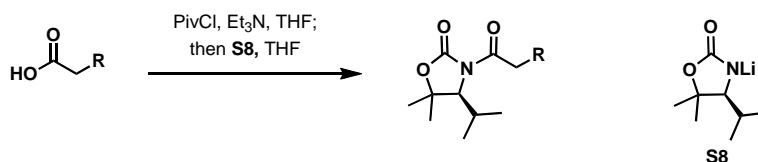
$[M]^+$ calcd for $C_{17}H_{23}NO_4$, 305.1627, found, 305.1637.



(S)-3-(2-(4-Fluorophenyl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.54).

The title compound was prepared from commercially available 4-fluorophenylacetyl chloride, (1.07 mL, 7.78 mmol) following standard procedure 1 for the synthesis of N-acyl oxazolidinones via acyl chloride and was obtained as a colorless oil (1.06 g, 3.61 mmol, 56%) after purification by column chromatography (silica, 9 ethyl acetate in hexanes - 13% ethyl acetate in hexanes). $\alpha_D^{27} + 45.86$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); δ (ppm): 7.32 (dd, $J = 8.1, 5.7$ Hz, 2H), 7.01 (dd, $J = 8.7$ Hz, 2H), 4.35 (d, $J = 15.1$ Hz, 1H), 4.20 (d, $J = 15.1$ Hz, 1H), 4.13 (d, $J = 3.1$ Hz, 1H), 2.14 – 2.06 (m, 1H), 1.50 (s, 3H), 1.32 (s, 3H), 0.95 (d, $J = 7.0$ Hz, 3H), 0.86 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); δ (ppm): 171.52 (s), 162.90 (s), 160.95 (s), 153.41 (s), 131.15 (d, $J = 8.0$ Hz), 129.63 (d, $J = 3.2$ Hz), 115.25 (d, $J = 21.4$ Hz), 82.87 (s), 66.39 (s), 40.61 (s), 29.50 (s), 28.65 (s), 21.36 (s), 21.23 (s), 16.74 (s); HRMS-ESI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{16}\text{H}_{20}\text{NO}_3$, 293.1427; found, 293.1435.

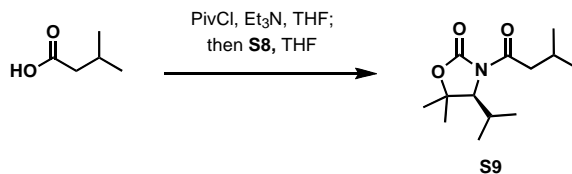
Standard procedure 2: Synthesis of *N*-acyl oxazolidinones via carboxylic acid



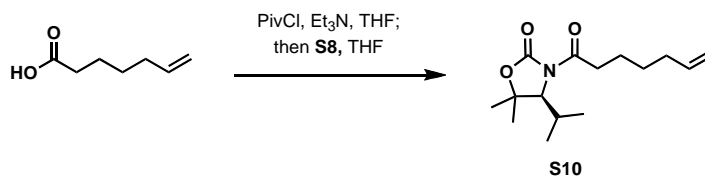
Solution A: Trimethylacetic acid chloroanhydride (1.45 equiv) was added to a solution of carboxylic acid (1.20 equiv) and triethylamine (4.80 equiv) in tetrahydrofuran (0.15 M) at -20°C . The solution was allowed to stir at -20°C for 2 h.

Solution B: In a separate flame-dried flask, *n*-butyllithium (1.10 equiv) was added to a solution of oxazolidione **S2** (1.00 equiv) in tetrahydrofuran (0.30 M) at -78°C and the mixture was allowed to warm to room temperature and stir for 30 min.

Both flasks were then chilled to -78°C . The flask containing the lithianted oxazolidione **S3** (**solution B**), was cannulated to the flask containing the mixed anhydride (**solution A**). After the addition was complete, the reaction mixture was warmed to room temperature and stirred for 3 h. The reaction was quenched with saturated ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 25 ml). The combined organic layers were washed with brine, dried over sodium sulfate, concentrated *in vacuo*, and purified by column chromatography to give the corresponding *N*-acyl oxazolidinone.

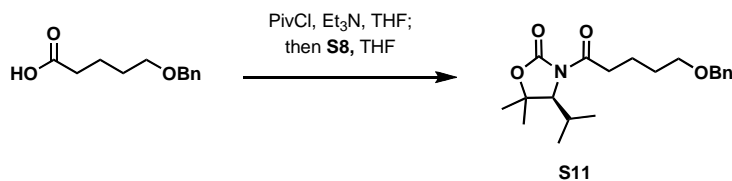


(S)-4-Isopropyl-5,5-dimethyl-3-(3-methylbutanoyl)oxazolidin-2-one (3.55). The title compound was prepared from commercially available 3-methylbutanoic acid (0.84 mL, 7.63 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as a colorless oil (1.34 g, 3.64 mmol, 88%) after purification by column chromatography (silica, 10 ethyl acetate in hexanes - 15% ethyl acetate in hexanes). $\alpha_D^{25} + 30.87$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 4.16 (d, $J = 3.2$ Hz, 1H), 2.91 (dd, $J = 15.6, 6.7$ Hz, 1H), 2.76 (dd, $J = 15.6, 7.1$ Hz, 1H), 2.25 – 2.16 (m, 1H), 2.14 (ddd, $J = 16.9, 8.5, 5.2$ Hz, 1H), 1.50 (s, 3H), 1.37 (s, 3H), 1.06 – 0.96 (m, 9H), 0.95 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 173.10 (s), 153.51 (s), 82.53 (s), 66.16 (s), 43.87 (s), 29.50 (s), 28.76 (s), 25.30 (s), 22.50 (s), 22.34 (s), 21.46 (s), 21.34 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{23}\text{NO}_3\text{Na}$, 264.1576; found, 264.1561.



(S)-3-(Hept-6-enoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.56). The title compound was prepared from commercially available 6-heptenoic acid (0.63 mL, 7.63 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as a colorless oil (1.53 g, 3.38 mmol, 90%) after

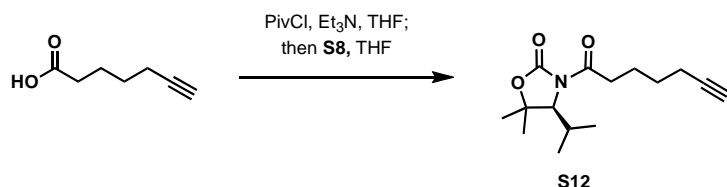
purification by column chromatography (silica, 9% ethyl acetate in hexanes). $\alpha_D^{26} + 32.15$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 5.78 (dddd, $J = 16.9, 10.2, 6.7$ Hz, 1H), 5.02 – 4.91 (m, 2H), 4.13 (d, $J = 3.3$ Hz, 1H), 2.99 (ddd, $J = 16.1, 8.5, 6.4$ Hz, 1H), 2.90 – 2.82 (m, 1H), 2.16 – 2.04 (m, 3H), 1.75 – 1.60 (m, 2H), 1.49 (s, 3H), 1.48 – 1.42 (m, 2H), 1.36 (s, 3H), 1.00 (d, $J = 7.0$ Hz, 3H), 0.92 (d, $J = 6.8$ Hz, 3H.); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 173.69 (s), 153.50 (s), 138.39 (s), 114.59 (s), 82.65 (s), 66.19 (s), 35.25 (s), 33.40 (s), 29.49 (s), 28.77 (s), 28.31 (s), 24.12 (s), 21.44 (s), 21.35 (s), 17.02 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{25}\text{NO}_3\text{Na}$, 290.1732; found, 290.1720.



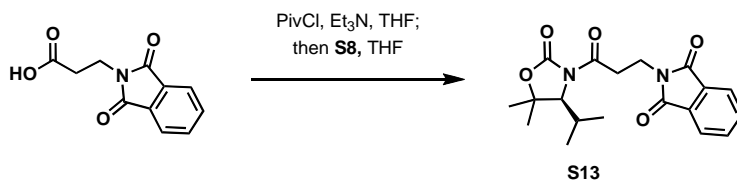
(S)-3-(5-(Benzyloxy)pentanoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.57).

The title compound was prepared from 6-heptenoic acid¹²⁴ (2.08 g, 10.0 mmol) following the standard procedure for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as a white solid (2.71 g, 7.81 mmol, 78%) after purification by column chromatography (silica, 15% ethyl acetate – hexanes). $\alpha_D^{26} + 24.09$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.33 (d, $J = 4.4$ Hz, 4H), 7.28 (dd, $J = 8.3, 4.1$ Hz, 1H), 7.25 (s, 1H), 4.50 (s, 2H), 4.14 (d, $J = 3.3$ Hz, 1H), 3.51 (t, $J = 6.2$ Hz, 2H), 3.03 (ddd, $J = 16.8, 8.1, 6.5$ Hz, 1H), 2.91 (ddd, $J = 16.8, 8.2, 6.3$ Hz, 1H), 2.13 (dddd, $J = 13.8, 6.9, 3.4$ Hz, 1H), 1.82 – 1.74 (m, 2H), 1.73 – 1.66 (m, 2H), 1.50 (s, 3H), 1.37 (s, 3H), 1.02 (d, $J = 7.0$ Hz, 3H), 0.93 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 173.58 (s), 153.54 (s),

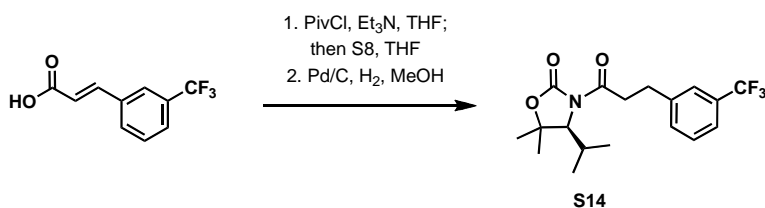
138.55 (s), 128.31 (s), 127.60 (s), 127.45 (s), 82.71 (s), 72.86 (s), 69.91 (s), 66.23 (s), 35.19 (s), 29.52 (s), 29.13 (s), 28.81 (s), 21.48 (s), 21.42 (s), 21.39 (s), 17.07 (s); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{29}NO_4Na$, 370.1994; found, 370.2002.



(S)-3-(Hept-6-ynoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.58). The title compound was prepared from commercially available 6-heptynoic acid (0.69 g, 5.42 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as a clear oil (1.41 g, 2.15 mmol, 75%) after purification by column chromatography (silica, 10 ethyl acetate in hexanes – 18% ethyl acetate in hexanes). $\alpha_D^{26} + 33.58$ (c 1.0, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$); δ (ppm): 4.15 (d, $J = 3.3$ Hz, 1H), 3.03 (ddd, $J = 16.6, 8.4, 6.5$ Hz, 1H), 2.91 (ddd, $J = 16.7, 8.3, 6.6$ Hz, 1H), 2.24 (ddd, $J = 7.1, 2.6$ Hz, 2H), 2.14 (dtd, $J = 13.8, 6.9, 3.4$ Hz, 1H), 1.95 (dd, $J = 2.6$ Hz, 1H), 1.86 – 1.74 (m, 2H), 2.14 (dtd, $J = 13.8, 6.9, 3.4$ Hz, 1H), 1.95 (dd, $J = 2.6$ Hz, 1H), 1.86 – 1.74 (m, 2H), 1.66 – 1.59 (m, 2H), 1.51 (s, 3H), 1.38 (s, 3H), 1.02 (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 173.37 (s), 153.51 (s), 83.96 (s), 82.73 (s), 68.51 (s), 66.22 (s), 34.92 (s), 29.49 (s), 28.80 (s), 27.86 (s), 23.69 (s), 21.45 (s), 21.36 (s), 18.21 (s), 17.04 (s); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{15}H_{23}NO_3Na$, 288.1576; found, 288.1571



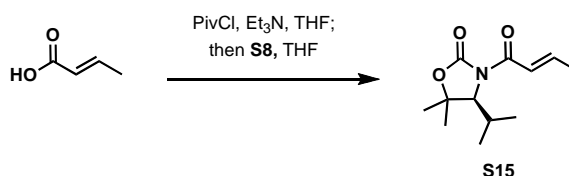
(S)-2-(3-(4-Isopropyl-5,5-dimethyl-2-oxooxazolidin-3-yl)-3-oxopropyl)isoindoline-1,3-dione (3.59). The title compound was prepared from commercially available 3-(1,3-Dioxo-1,3-dihydro-2H-isoindol-2-yl)-propanoic acid (8.69 g, 39.7 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as a white solid (6.78 g, 18.9 mmol, 48%) after purification by column chromatography (silica, 20 ethyl acetate in hexanes - 25% ethyl acetate in hexanes); $\alpha_D^{26} + 18.79$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.86 – 7.83 (m, 2H), 7.73 – 7.69 (m, 2H), 4.13 (d, *J* = 3.2 Hz, 1H), 4.09 – 4.05 (m, 2H), 3.43 – 3.35 (m, 1H), 3.29 (ddd, *J* = 17.1, 7.5 Hz, 1H), 2.14 (ddd, *J* = 13.9, 6.9, 3.2 Hz, 1H), 1.51 (s, 3H), 1.44 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 170.79 (s), 167.96 (s), 153.43 (s), 133.91 (s), 132.00 (s), 123.21 (s), 83.15 (s), 66.30 (s), 34.24 (s), 33.44 (s), 29.48 (s), 28.78 (s), 21.41 (s), 21.21 (s), 16.95 (s); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₉H₂₂N₂O₅Na, 381.1426; found, 381.1427.



(S)-4-Isopropyl-5,5-dimethyl-3-(3-(3-(trifluoromethyl)phenyl)propanoyl)oxazolidin-2-one (3.60). The title compound was prepared starting from commercially available 3-trifluoromethylcinnamic acid (1.65 g, 7.63 mmol) following standard procedure 2 for the

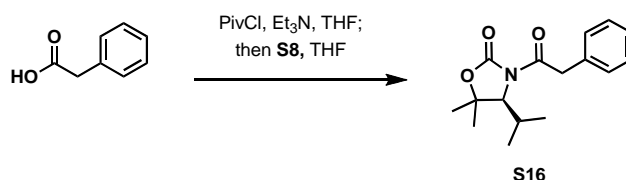
synthesis of N-acyl oxazolidinones via carboxylic acid without purification. The resultant oil was then submitted to the next reaction.

The crude substrate and palladium on carbon (0.20 g) were mixed in ethanol (28.0 mL, 0.2 M). Hydrogen gas was then bubbled through the reaction mixture for 15 min at rt. The reaction mixture flask was pressurized with hydrogen gas and the reaction was stirred for 3h at rt. The reaction mixture was filtered through Celite and the solvent was removed *in vacuo*. The title compound was obtained as a clear oil (1.98 g, 5.54 mmol, 88%) after purification by column chromatography (silica, 15% ethyl acetate in hexanes). $\alpha_D^{26} + 25.37$ (*c* 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.50 (s, 1H), 7.45 (d, *J* = 7.7 Hz, 2H), 7.41 – 7.37 (m, 1H), 4.13 (d, *J* = 3.4 Hz, 1H), 3.37 (ddd, *J* = 16.9, 8.6, 6.6 Hz, 1H), 3.24 (ddd, *J* = 16.9, 8.2, 6.7 Hz, 1H), 3.14 – 2.99 (m, 2H), 2.11 (dddd, *J* = 13.8, 6.9, 3.4 Hz, 1H), 1.49 (s, 3H), 1.32 (s, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 172.39 (s), 153.50 (s), 141.40 (s), 131.99 (d, *J* = 1.3 Hz), 130.69 (q, *J* = 32.0 Hz), 128.84 (s), 125.22 (q, *J* = 3.8 Hz), 123.23 – 122.77 (m), 82.94 (s), 66.34 (s), 36.58 (s), 30.34 (s), 29.46 (s), 28.70 (s), 21.35 (s), 21.33 (s), 16.96 (s); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₈H₂₂F₃NO₃Na, 380.1449; found, 380.1450.



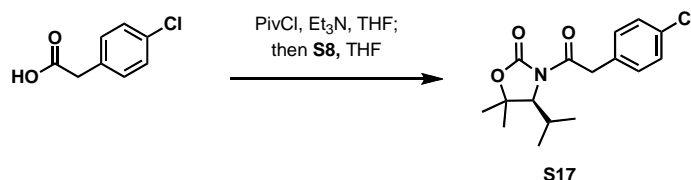
(*S,E*)-3-(But-2-enoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.61). The title compound was prepared from commercially available crotonic acid (0.517 g, 6.00 mmol)

following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as a white solid (0.770 g, 3.42 mmol, 68%) after purification by column chromatography (silica, 10 ethyl acetate in hexanes - 30% ethyl acetate in hexanes). $\alpha_D^{26} + 52.90$ (*c* 1.0, CHCl₃). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.29 (ddd, *J* = 15.2, 3.2, 1.5 Hz, 1H), 7.12 (dddd, *J* = 15.1, 6.9 Hz, 1H), 4.19 (d, *J* = 3.4 Hz, 1H), 2.13 (dddd, *J* = 13.8, 6.9, 3.5 Hz, 1H), 1.93 (dd, *J* = 6.9, 1.6 Hz, 3H), 1.49 (s, 3H), 1.36 (s, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 165.54 (s), 153.48 (s), 146.44 (s), 121.88 (s), 82.63 (s), 66.23 (s), 29.60 (s), 28.73 (s), 21.37 (s), 21.33 (s), 18.40 (s), 17.03 (s); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₂H₁₉NO₃Na, 248.1263; found, 248.1255.



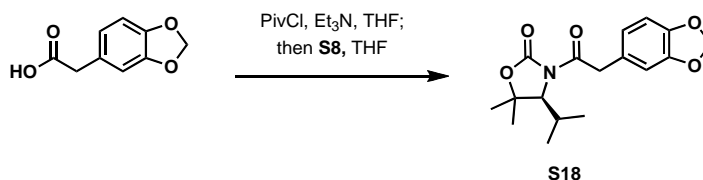
(S)-4-Isopropyl-5,5-dimethyl-3-(2-phenylacetyl)oxazolidin-2-one (3.62). The title compound was prepared from commercially available phenyl acetic acid (1.51 g, 11.1 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as yellow oil (2.24 g, 8.1 mmol, 81%) after purification by column chromatography (silica, 15% ethyl acetate – hexanes. $\alpha_D^{26} + 36.65$ (*c* 0.7, CHCl₃); ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.36 – 7.30 (m, 4H), 7.27 (dd, *J* = 1.9 Hz, 1H), 7.26 – 7.24 (m, 1H), 4.37 (d, *J* = 15.0 Hz, 1H), 4.26 (d, *J* = 15.0 Hz, 1H), 4.13 (d, *J* = 3.3 Hz, 1H), 2.11 (dddd, *J* = 13.8, 6.9, 3.3 Hz, 1H), 1.49 (s, 3H), 1.31 (s, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 171.77 (s), 153.53 (s), 133.99

(s), 129.64 (s), 128.50 (s), 127.12 (s), 82.86 (s), 66.51 (s), 41.56 (s), 29.60 (s), 28.76 (s), 21.43 (s), 21.37 (s), 16.86 (s); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{16}H_{21}NO_3Na$ 298.1419; found, 298.1414.



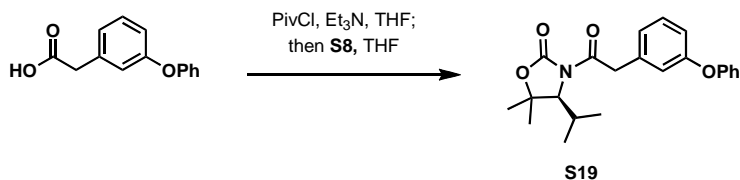
(S)-3-(2-(4-Chlorophenyl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.63).

The title compound was prepared from commercially available 2-(4-chlorophenyl)acetic acid (1.30 g, 7.63 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as green solid (0.54 g, 1.7 mmol, 28%) after purification by column chromatography (silica, 20 - 25% ethyl acetate in hexanes). $\alpha_D^{27} + 37.17$ (c 1.0, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.29 (d, $J = 2.0$ Hz, 4H), 4.35 (d, $J = 15.1$ Hz, 1H), 4.20 (d, $J = 15.1$ Hz, 1H), 4.13 (d, $J = 3.2$ Hz, 1H), 2.14 – 2.06 (m, 1H), 1.50 (s, 3H), 1.33 (s, 3H), 0.96 (d, $J = 7.0$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 171.05 (s), 153.28 (s), 132.83 (s), 132.34 (s), 130.87 (s), 128.44 (s), 82.81 (s), 66.30 (s), 40.70 (s), 29.41 (s), 28.57 (s), 21.31 (s), 21.14 (s), 16.69 (s); HRMS-EI (m/z): $[M]^+$ calcd for $C_{16}H_{20}ClNO_3$, 309.1132; found, 309.1132.



(S)-3-(2-(Benzo[d][1,3]dioxol-5-yl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one

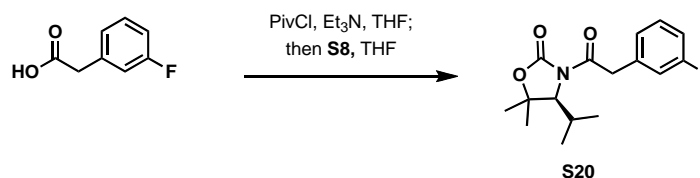
(3.64). The title compound was prepared from commercially available 2-(benzo[1,3]dioxol-5-yl)acetic acid (1.65 g, 7.63 mmol) following standard procedure 2 for the synthesis of *N*-acyl oxazolidinones via carboxylic acid and was obtained as white solid (1.43 g, 4.45 mmol, 71%) after purification by column chromatography (silica, 11% ethyl acetate in hexanes). $\alpha_D^{23} + 39.58$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 6.84 (d, *J* = 1.3 Hz, 1H), 6.81 – 6.78 (m, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 5.93 (s, 2H), 4.27 (d, *J* = 15.1 Hz, 1H), 4.17 (s, 1H), 4.13 (d, *J* = 3.2 Hz, 1H), 2.15 – 2.07 (m, 1H), 1.50 (s, 3H), 1.33 (s, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 171.81 (s), 153.47 (s), 147.62 (s), 146.64 (s), 127.50 (s), 122.75 (s), 110.09 (s), 108.20 (s), 100.91 (s), 82.85 (s), 66.45 (s), 41.06 (s), 29.55 (s), 28.75 (s), 21.42 (s), 21.32 (s), 16.85 (s); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₇H₂₁NO₅Na, 342.1317; found, 342.1306.



(S)-4-Isopropyl-5,5-dimethyl-3-(2-(3-phenoxyphenyl)acetyl)oxazolidin-2-one (3.65).

The title compound was prepared from commercially available 2-(3-phenoxyphenyl)acetic acid (0.326 g, 1.43 mmol) following standard procedure 2 for the synthesis of *N*-acyl oxazolidinones via carboxylic acid and was obtained as yellow oil (0.36 g, 0.98 mmol, 76%) after purification by column chromatography (silica, 12% ethyl acetate in hexanes). $\alpha_D^{22} + 52.08$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.34 – 7.26 (m, 3H), 7.09 (dd, *J* = 7.4 Hz, 2H), 7.02 – 6.97 (m, 3H), 6.91 (dd, *J* = 8.1, 1.9 Hz, 1H), 4.36 (d, *J* = 15.1 Hz, 1H),

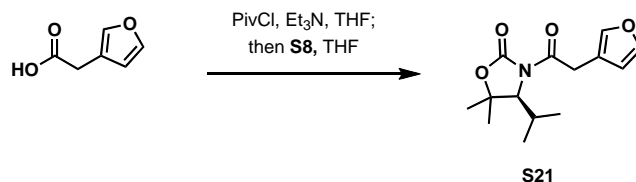
4.22 (d, $J = 15.1$ Hz, 1H), 4.14 (d, $J = 3.2$ Hz, 1H), 2.11 (dddd, $J = 13.8, 6.9, 3.3$ Hz, 1H), 1.49 (s, 3H), 1.33 (s, 3H), 0.97 (d, $J = 7.0$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 171.28 (s), 157.21 (s), 157.08 (s), 153.40 (s), 129.67 (s), 129.64 (s), 124.55 (s), 123.14 (s), 120.14 (s), 118.79 (s), 117.55 (s), 82.85 (s), 66.42 (s), 41.37 (s), 29.55 (s), 28.74 (s), 21.40 (s), 21.31 (s), 16.85 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_4\text{Na}$, 390.1681; found, 390.1698.



(S)-3-(2-(3-Fluorophenyl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.66)

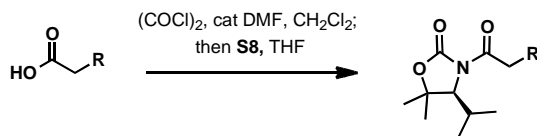
The title compound was prepared from commercially available 2-(3-fluorophenyl)acetic acid (1.17 g, 7.60 mmol) following standard procedure 2 for the synthesis of N-acyloxazolidinones via carboxylic acid and was obtained as yellow oil (1.46 g, 4.97 mmol, 79%) after purification by column chromatography (silica, 12% ethyl acetate in hexanes). $\alpha_{\text{D}}^{23} + 48.61$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.30 – 7.26 (m, 1H), 7.25 (s, 1H), 7.11 (dd, $J = 7.7, 0.4$ Hz, 1H), 7.08 – 7.04 (m, 1H), 6.98 – 6.93 (m, 1H), 4.37 (d, $J = 15.1$ Hz, 1H), 4.23 (d, $J = 15.1$ Hz, 1H), 4.13 (d, $J = 3.3$ Hz, 1H), 2.11 (dddd, $J = 13.8, 6.9, 3.3$ Hz, 1H), 1.49 (s, 3H), 1.33 (s, 3H), 0.96 (d, $J = 7.0$ Hz, 3H), 0.87 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 171.07 (s), 162.71 (d, $J = 245.8$ Hz), 153.44 (s), 136.24 (d, $J = 7.9$ Hz), 129.86 (d, $J = 8.4$ Hz), 125.33 (d, $J = 3.1$ Hz), 116.62 (d, $J = 21.8$ Hz), 114.08 (d, $J = 21.0$ Hz), 82.97 (s), 66.49 (s), 41.20 (d, $J = 2.0$ Hz), 29.55 (s), 28.74 (s),

21.41 (s), 21.31 (s), 16.83 (s); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{16}H_{20}FNO_3Na$, 316.1325; found, 316.1324.



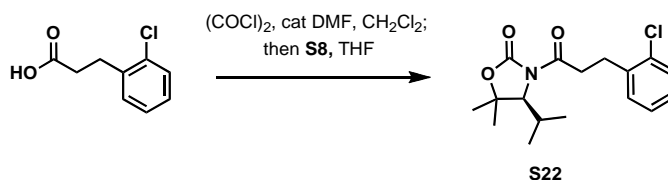
(S)-3-(2-(Furan-3-yl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.67) The title compound was prepared from commercially available 3-furylacetic acid (0.191 g, 1.51 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained after purification by column chromatography (silica, 20% ethyl acetate in hexanes) as a clear oil (0.266 g, 1.00 mmol, 66%). $\alpha_D^{21} + 39.04$ (c 1.0, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.41 (d, $J = 0.5$ Hz, 1H), 7.34 (t, $J = 1.6$ Hz, 1H), 6.37 (d, $J = 1.1$ Hz, 1H), 4.13 (d, $J = 16.0$ Hz, 1H), 4.10 (d, $J = 3.2$ Hz, 1H), 4.04 (d, $J = 16.0$ Hz, 1H), 2.09 (dtd, $J = 13.8, 6.9, 3.3$ Hz, 1H), 1.46 (s, 3H), 1.30 (s, 3H), 0.95 (d, $J = 7.0$ Hz, 3H), 0.86 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 171.04 (s), 153.34 (s), 142.69 (s), 140.89 (s), 117.09 (s), 111.33 (s), 82.82 (s), 66.28 (s), 31.63 (s), 29.45 (s), 28.59 (s), 21.31 (s), 21.19 (s), 16.71 (s). LRMS (m/z): $[M+Na]^+$ calcd for $C_{15}H_{23}NO_3Na$, 288.12; found, 288.15.

Standard procedure 3: Synthesis of *N*-acyl oxazolidinones via acyl chloride from carboxylic acid



Oxalyl chloride (1.65 equiv) was added to a solution of carboxylic acid (1.50 equiv), dimethylformamide (10 μ l), and dichloromethane (2.0 M) at 0 °C. After 10 min, the solution was warmed to rt and stirred for 45 min (or until bubbling stops). The solution was concentrated on a rotary evaporator.

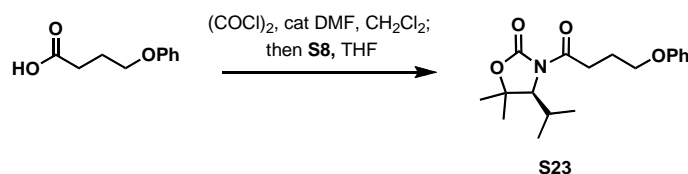
In a separate flask, *n*-butyllithium (1.05 equiv), was added to a solution of oxazolidinone **S2** (1.00 equiv) in THF (0.35 M) at -78 °C under argon. The solution was stirred for 30 min at -78 °C. A solution of the crude acyl chloride in THF (0.6 M total, 3 rinses) was added dropwise at -78 °C. After stirring at -78 °C for 2 h, the reaction mixture was warmed to rt and stirred for 2 h. The reaction mixture was quenched with saturated aqueous ammonium chloride. The layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo*. The resultant oil or solid was purified by column chromatography to give the corresponding *N*-acyl oxazolidinone.



(*S*)-3-(3-(2-Chlorophenyl)propanoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one

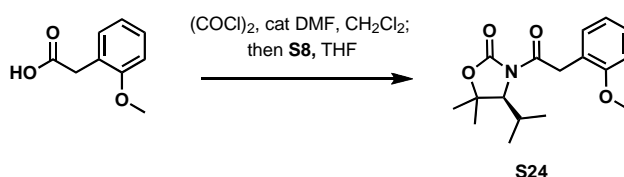
(3.68). The title compound was prepared from commercially available 3-(2-

Chlorophenyl)propanoic acid (1.29 g, 7.00 mmol) following the standard procedure for the synthesis of *N*-acyl oxazolidinones via acyl chloride from carboxylic acid and was obtained as a yellow oil (1.77 g, 5.46 mmol, 74%) after purification by column chromatography (silica, 15% ethyl acetate in hexanes). $\alpha_D^{26} + 30.14$ (*c* 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.36 – 7.27 (m, 2H), 7.16 (ddd, *J* = 13.5, 10.5, 6.2 Hz, 2H), 4.15 (d, *J* = 3.1 Hz, 1H), 3.38 – 3.20 (m, 2H), 3.12 (dt, *J* = 9.0, 6.0 Hz, 2H), 2.14 (ddd, *J* = 10.3, 8.3, 5.1 Hz, 1H), 1.50 (s, 3H), 1.36 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.94 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ (ppm): 172.66 (s), 153.47 (s), 138.05 (s), 134.00 (s), 130.50 (s), 129.48 (s), 127.71 (s), 126.80 (s), 82.85 (s), 66.36 (s), 35.15 (s), 29.49 (s), 28.83 (s), 28.34 (s), 21.40 (s), 17.07 (s). HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₇H₂₂ClNO₃Na, 346.1186; found, 346.1189.



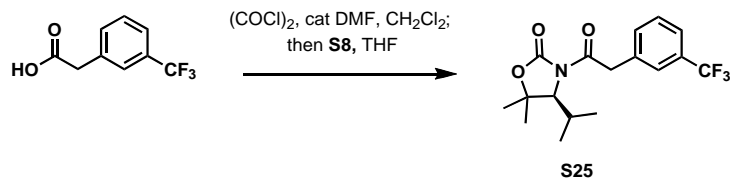
(S)-4-Isopropyl-5,5-dimethyl-3-(4-phenoxybutanoyl)oxazolidin-2-one (3.69). The title compound was prepared from commercially available 4-phenoxybutanoic acid (2.70 g, 15.0 mmol) following the standard procedure for the synthesis of *N*-acyl oxazolidinones via acyl chloride from carboxylic acid and was obtained as a white solid (2.95 g, 0.92 mmol, 92%) after purification by column chromatography (silica, 5 -25% ethyl acetate in hexanes). $\alpha_D^{26} + 29.90$ (*c* 1.0, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.29 – 7.27 (m, 1H), 7.25 (dd, *J* = 4.7, 2.6 Hz, 1H), 6.95 – 6.88 (m, 3H), 4.15 (d, *J* = 3.4 Hz, 1H), 4.04 (dd, *J* = 6.2 Hz, 2H), 3.16 (dddd, *J* = 17.5, 7.8, 6.8 Hz, 2H), 2.22 – 2.11 (m, 3H), 1.50 (s, 3H), 1.37 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃);

$\delta(\text{ppm})$: 173.16 (s), 158.80 (s), 153.51 (s), 129.35 (s), 120.61 (s), 114.50 (s), 82.82 (s), 66.58 (s), 66.31 (s), 32.11 (s), 29.51 (s), 28.81 (s), 28.81 (s), 24.22 (s), 21.44 (s), 21.37 (s), 17.05 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_4\text{Na}$, 342.1681; found, 342.1679.

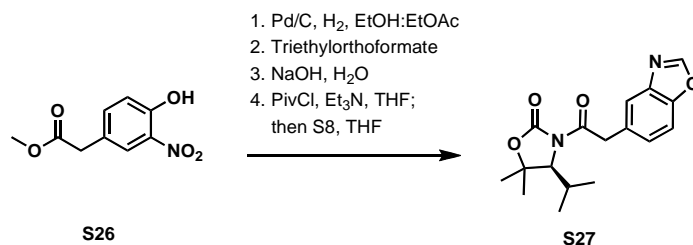


(S)-4-Isopropyl-3-(2-(2-methoxyphenyl)acetyl)-5,5-dimethyloxazolidin-2-one (3.70).

The title compound was prepared from commercially available 2-(2-methoxyphenyl)acetic acid (0.73 g, 4.00 mmol) following standard procedure 3 for the synthesis of N-acyl oxazolidinones via acyl chloride from carboxylic acid and was obtained as white solid (0.51 g, 1.67 mmol, 42%) after purification by column chromatography (silica, 15% ethyl acetate in hexanes). $\alpha_D^{26} + 25.03$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.28 (d, $J = 1.5$ Hz, 1H), 7.25 (d, $J = 1.7$ Hz, 1H), 7.17 (d, $J = 7.3$ Hz, 1H), 6.92 (dd, $J = 7.1$ Hz, 1H), 6.87 (d, $J = 8.2$ Hz, 1H), 4.25 (ddd, $J = 17.3$ Hz, 2H), 4.17 (d, $J = 3.2$ Hz, 1H), 3.78 (s, 3H), 2.18 – 2.12 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H), 1.02 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 171.74 (s), 157.36 (s), 153.77 (s), 131.16 (s), 128.50 (s), 123.31 (s), 120.46 (s), 110.26 – 109.82 (m), 82.80 (s), 66.50 (s), 55.26 (s), 37.19 (s), 29.57 (s), 28.69 (s), 21.51 (s), 21.31 (d, $J = 6.5$ Hz), 16.89 (s); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_4\text{Na}$, 328.1525; found, 328.1522.



(S)-4-Isopropyl-5,5-dimethyl-3-(2-(3-(trifluoromethyl)phenyl)acetyl)oxazolidin-2-one (3.71). The title compound was prepared from commercially available 2-(3-trifluoromethyl)acetic acid (1.71 g, 8.40 mmol) following standard procedure 3 for the synthesis of N-acyl oxazolidinones via acyl chloride from carboxylic acid and was obtained as yellow oil (1.01 g, 2.94 mmol, 35%) after purification by column chromatography (silica, 30% ethyl acetate – hexanes). $\alpha_D^{23} + 33.10$ (*c* 0.1, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.59 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 2H), 7.44 (dd, *J* = 7.7 Hz, 1H), 4.44 (d, *J* = 15.4 Hz, 1H), 4.29 (d, *J* = 15.4 Hz, 1H), 4.15 (d, *J* = 3.2 Hz, 1H), 2.15 – 2.09 (m, 1H), 1.50 (s, 3H), 1.50 (s, 3H), 1.34 (s, 3H), 1.34 (s, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 170.90 (s), 153.44 (s), 134.90 (s), 133.25 (d, *J* = 1.2 Hz), 131.31 – 130.18 (m), 128.88 (d, *J* = 7.3 Hz), 126.29 (q, *J* = 3.8 Hz), 124.00 (q, *J* = 3.8 Hz), 124.00 (d, *J* = 272.2 Hz), 83.07, (s), 66.52 (s), 41.34 (s), 29.57 (s), 28.75 (s), 21.38 (s), 21.31 (s), 16.81 (s); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₇H₂₀F₃NO₃Na, 366.1293; found, 366.1292.



(S)-3-(2-(benzo[d]oxazol-5-yl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one

(3.73) The title compound was prepared starting from known methyl ester **3.72**¹²⁵ using the following procedure.

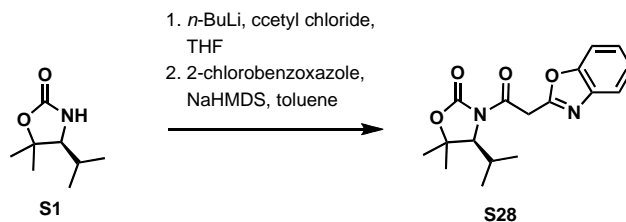
Pd/C (20 mol %) was added to a solution of **3.72** (1.37 g, 6.48 mmol) in a 1:1 mixture of EtOH/EtOAc (0.16 M). The reaction mixture was placed under an atmosphere of H₂ and stirred for 14 h. The reaction mixture was then filtered through a pad of celite and the remaining residue was washed using a solvent system of 1:1 EtOH and EtOAc. The filtrate was concentrated in *vacuo* providing a dark brown solid (1.08 g, 99%). The crude product was used without further purification

Triethylorthoformate (13.3 mL, 0.8 M) was added to the crude substrate (10.6 mmol) and the mixture was heated at reflux for 18 h. The reaction mixture was then transferred to a separatory funnel containing water (90 mL) and extracted with ethyl acetate (3 x 15 mL). The organic layer was dried over Na₂SO₄ and concentrated in *vacuo* providing a light brown oil (1.75 g, 10.5 mmol, 99%). The crude product was used without further purification.

An aqueous solution of NaOH was added (0.4 M, 11.36 mmol, 1.2 equiv) to a solution of crude substrate (1.81 g, 9.47 mmol) in methanol (0.37 M) and the mixture was stirred for 12 h. The reaction mixture was diluted with H₂O to a concentration of 0.035 M. Concentrated aqueous HCl was added until a pH of ~4 was achieved. The solution was

allowed to stir for 1 h and the solids were collected by filtration and washed with cold water providing the product as a crude tan solid (0.673 g, 3.52 mmol, 41%).

The title compound was prepared from the solid collected (0.375 g, 2.11 mmol) following standard procedure 2 for the synthesis of N-acyl oxazolidinones via carboxylic acid and was obtained as white solid (0.433 g, 1.37 mmol, 65%) after purification by column chromatography (silica, 24% ethyl acetate to 30% ethyl acetate in hexanes). $\alpha_D^{21} + 29.80$ (c 1.0, CHCl_3). ^1H NMR (600 MHz, CDCl_3) δ (ppm): 8.05 (s, 1H), 7.73 (s, 1H), 7.49 (d, $J = 8.4$ Hz, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 4.47 (d, $J = 15.4$ Hz, 1H), 4.33 (d, $J = 15.4$ Hz, 1H), 4.11 (d, $J = 3.1$ Hz, 1H), 2.11 – 2.03 (m, 1H), 1.45 (s, 3H), 1.29 (s, 3H), 0.92 (d, $J = 7.0$ Hz, 3H), 0.83 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ (ppm): 171.51 (s), 153.38 (s), 152.77 (s), 149.04 (s), 140.20 (s), 130.55 (s), 127.25 (s), 121.47 (s), 110.62 (s), 82.86 (s), 66.37 (s), 41.27 (s), 29.44 (s), 28.67 (s), 21.35 (s), 21.21 (s), 16.77 (s). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_4\text{Na}$, 339.1321; found, 339.1314.



(S)-3-(2-(benzo[d]oxazol-2-yl)acetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one

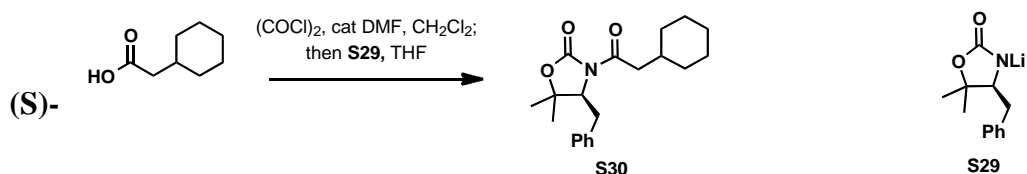
(3.74) The title compound was prepared starting from oxazolidone **S2** using the following procedure.

To a solution of **S2** (1.5 g, 9.54 mmol) in THF (0.3 M) at -78 °C, *n*-BuLi (4.5 mL, 2.33 M in hexanes, 10.5 mmol, 1.1 equiv) was added dropwise. After the addition was complete,

the reaction mixture was warmed to room temperature and stirred for 30 min. The reaction mixture was chilled to -78 °C and acetyl chloride (0.82 mL, 11.45 mmol, 1.2 equiv) was added. After the addition was complete, the reaction mixture was warmed to room temperature and stirred for 12 h. The reaction was quenched with saturated ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine, dried over sodium sulfate, concentrated *in vacuo*. (S)-3-acetyl-4-isopropyl-5,5-dimethyloxazolidin-2-one was obtained after purification by column chromatography (silica, 12% ethyl acetate to 14% ethyl acetate in hexanes) as a colorless oil (1.4 g, 7.03 mmol, 74%).

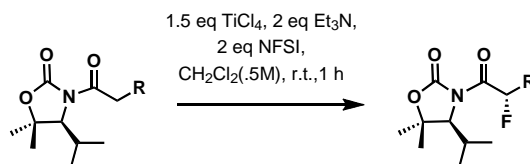
To a solution of (S)-3-acetyl-4-isopropyl-5,5-dimethyloxazolidin-2-one (0.500 g, 2.50 mmol) and 2-chlorobenzoxazole (0.385 g, 2.50 mmol) in toluene (11 mL) at 0 °C, NaHMDS (0.6 M in toluene, 8.3 mL, 5 mmol, 2 equiv) was added dropwise. After the addition was complete, the reaction mixture was allowed to stir at 0 °C for 2 h and then warmed to room temperature and stirred 12 h. The reaction was quenched with 1N NH₄Cl solution (38 mL, 15.3 equiv). The organic layer was separated and collected. The aqueous layer was extracted with EtOAc (3 x 15 mL), the combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo*. The title compound was obtained after purification by column chromatography (silica, 21% ethyl acetate to 25% ethyl acetate in hexanes) as a green solid (0.510 g, 1.61 mmol, 65%). $\alpha_D^{20} + 49.79$ (*c* 1.0, CHCl₃). ¹H NMR (600 MHz, CDCl₃) δ (ppm): 7.68 – 7.64 (m, 1H), 7.48 (d, *J* = 5.0 Hz, 1H), 7.32 – 7.27 (m, 2H), 4.73 (d, *J* = 17.1 Hz, 1H), 4.55 (d, *J* = 17.1 Hz, 1H), 4.20 (d, *J* = 2.5 Hz, 1H), 2.21 – 2.15 (m, 1H), 1.52 (d, *J* = 6.3 Hz, 3H), 1.47 (s, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ (ppm): 166.63 (s), 159.96 (d, *J* = 0.9 Hz), 153.40 (s), 151.02 (s),

141.07 (s), 124.88 (s), 124.21 (s), 119.85 (s), 110.48 (s), 83.63 (s), 66.76 (s), 36.75 (s), 29.56 (s), 28.74 (s), 21.42 (s), 21.30 (s), 16.85 (s). HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{17}H_{20}N_2O_4Na$, 339.1321; found, 339.1331.



3-(2-Cyclohexylacetyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (3.75). The title compound was prepared from commercially available 2-cyclohexylacetic acid following known literature protocols by Herrmann *et al.* ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.32 – 7.26 (m, 4H), 7.26 – 7.25 (m, 1H), 7.22 (ddd, $J = 8.5, 3.8, 1.8$ Hz, 1H), 4.51 (dd, $J = 9.6, 3.9$ Hz, 1H), 3.13 (dd, $J = 14.4, 3.8$ Hz, 1H), 2.91 – 2.75 (m, 3H), 1.88 – 1.78 (m, 1H), 1.74 – 1.60 (m, 5H), 1.36 (s, 3H), 1.34 (s, 3H), 1.31 – 1.21 (m, 2H), 1.18 – 1.10 (m, 1H), 1.04 – 0.95 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 172.78 (s), 152.58 (s), 136.96 (s), 129.02 (s), 128.59 (s), 126.71 (s), 81.92 (s), 77.25 (s), 77.00 (s), 76.75 (s), 63.46 (s), 42.68 (s), 35.39 (s), 34.44 (s), 33.01 (d, $J = 10.0$ Hz), 28.50 (s), 26.11 (d, $J = 10.4$ Hz), 22.24 (s).

Standard procedure for α -monofluorination of N -acyl oxazolidinones:



The substrate (0.50 mmol, 1.00 equiv) was charged to a flame dried 10 ml round bottom flask or 1 dram vial. The reaction vessel was then backfilled with argon 3 times. Next,

dichloromethane (0.50 M) was added and the solution was then cooled to 0 °C. A solution of TiCl₄ (1.00 M in CH₂Cl₂, 0.75 mL, 0.75 mmol, 1.50 equiv) was added dropwise to the reaction mixture at 0 °C and the mixture was stirred for 5 min. Triethylamine (0.14 mL, 1.00 mmol, 2.00 equiv) was added and the reaction mixture was stirred at 0 °C for 30 min. *N*-Fluorobenzenesulfonimide (NFSI, 0.315 g, 2.00 mmol, 2.00 equiv) was then added to the reaction mixture in one portion at 0 °C (CAUTION: reaction may bubble vigorously upon addition). The reaction was then warmed to rt and stirred for 1 h. The reaction mixture was filtered through a 1.5 cm silica gel plug, and the silica plug was washed with dichloromethane (5 mL) and ethyl acetate (40 mL). The combined filtrate was concentrated *in vacuo* and the residue purified by flash column chromatography to give the corresponding α -monofluorinated *N*-acyl oxazolidinone.

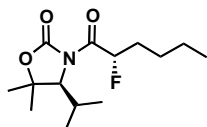


Table 3.5.3, entry 1. The title compound was prepared from oxazolidinone **3.49** (0.128 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 15% ethyl acetate in hexanes) to afford product as a colorless oil (0.128 g, 0.47 mmol, 94%, single diastereomer). α -D₂₄ + 13.60 (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 5.99 (d, *J* = 51.4 Hz, 1H), 4.10 (d, *J* = 3.0 Hz, 1H), 2.20 (dddd, *J* = 13.8, 6.9, 3.1 Hz, 1H), 1.87 – 1.76 (m, 2H), 1.53 (s, 3H), 1.52 – 1.45 (m, 1H), 1.41 (dd, *J* = 13.2, 7.8 Hz, 1H), 1.39 (s, 3H), 1.38 – 1.30 (m, 1H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.91 (dd, *J* = 7.3 Hz, 3H); ¹³C NMR (151 MHz,

CDCl₃); δ (ppm): 170.50 (d, $J = 22.7$ Hz), 153.08 (s), 89.14 (d, $J = 178.5$ Hz), 84.01 (s), 66.87 (s), 32.04 (d, $J = 22.1$ Hz), 29.47 (s), 28.95 (s), 26.90 (d, $J = 1.9$ Hz), 22.13 (s), 21.40 (s), 21.31 (s), 16.98 (s), 13.82 (s); ¹⁹F NMR (564 MHz, CDCl₃); δ (ppm): -192.24 – -192.48 (m, 1F); HRMS-ESI (m/z): [M+Na]⁺ calcd for C₁₄H₂₄FNO₃Na, 296.1638; found, 296.1633.

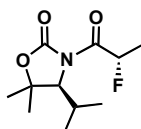


Table 3.5.3, entry 2. The title compound was prepared from oxazolidinone **3.50** (0.107 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 11% ethyl acetate in hexanes) to afford product as a white solid (0.105 g, 0.46 mmol, 91%, single diastereomer. $\alpha_D^{26} + 14.78$ (c 0.42, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 6.08 (dddd, $J = 49.2, 6.5$ Hz, 1H), 4.11 (d, $J = 3.2$ Hz, 1H), 2.19 (dddd, $J = 13.9, 7.0, 3.2$ Hz, 1H), 1.57 (dd, $J = 23.8, 6.5$ Hz, 3H), 1.53 (s, 3H), 1.39 (s, 3H), 1.06 (d, $J = 7.0$ Hz, 3H), 0.97 (d, $J = 6.9$ Hz, 3H); ¹³C NMR (201 MHz, CDCl₃); δ (ppm): 172.79 (d, $J = 22.4$ Hz), 154.80 (s), 87.58 (d, $J = 176.6$ Hz), 85.87 (s), 68.62 (s), 31.27 (s), 30.74 (s), 23.16 (s), 23.11 (s), 19.90 (d, $J = 23.6$ Hz), 18.73 (s); ¹⁹F NMR (564 MHz, CDCl₃); δ (ppm): -183.56 - -183.80 (m, 1F). HRMS-ESI (m/z): [M+Na]⁺ calcd for C₁₁H₁₈FNO₃Na, 254.1168; found, 254.1164.

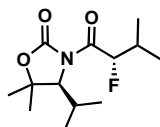


Table 3.5.3, entry 3. The title compound was prepared from oxazolidinone **3.55** (0.121 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr >98:2) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 6% ethyl acetate in hexanes) to afford product as a colorless oil (0.100 g, 0.39 mmol, 77%, single diastereomer). α $^{26}_{\text{D}}$ + 42.22 (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); δ (ppm): 5.89 (dd, J = 49.6, 3.2 Hz, 1H), 4.11 (d, J = 3.0 Hz, 1H), 2.23 – 2.11 (m, 2H), 1.53 (s, 3H), 1.38 (s, 3H), 1.11 (d, J = 6.9 Hz, 3H), 1.08 (d, J = 7.0 Hz, 3H), 0.97 (dd, J = 6.6 Hz, 6H); ^{13}C NMR (151 MHz, CDCl_3); δ (ppm): 169.73 (d, J = 23.0 Hz), 153.12 (s), 92.31 (dd, J = 181.2, 19.7 Hz), 83.86 (s), 67.03 (d, J = 19.1 Hz), 30.63 (t, J = 20.2 Hz), 29.49 (d, J = 19.9 Hz), 28.86 (d, J = 11.6 Hz), 21.40 (d, J = 6.6 Hz), 21.24 (s), 18.85 (d, J = 18.9 Hz), 16.98 (d, J = 17.4 Hz), 15.26 (d, J = 16.3 Hz); ^{19}F NMR (564 MHz, CDCl_3); δ (ppm): -204.40 (dd, J = 50.2, 28.3 Hz, 1F). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{22}\text{FNO}_3\text{Na}$, 282.1481; found, 282.1489.

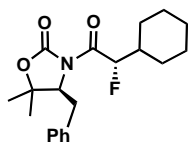


Table 3.5.3, entry 4. The title compound was prepared from oxazolidinone **3.75** (0.165 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 96:4) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 20% ethyl acetate in hexanes - 25%

ethyl acetate in hexanes) to afford product as a white solid (0.160 g, 0.46 mmol, 92%, single diastereomer). $\alpha_D^{26} + 19.05$ (*c* 0.42, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.33 – 7.27 (m, 4H), 7.24 (dd, *J* = 7.1 Hz, 1H), 5.83 (dd, *J* = 49.6, 3.6 Hz, 1H), 4.46 (dd, *J* = 9.9, 3.0 Hz, 1H), 3.25 (dd, *J* = 14.5, 2.8 Hz, 1H), 2.93 (dd, *J* = 14.5, 9.9 Hz, 1H), 1.84 (dddd, *J* = 58.1, 34.1, 16.5, 8.1 Hz, 4H), 1.65 (dd, *J* = 21.0, 12.8 Hz, 2H), 1.44 – 1.35 (m, 7H), 1.35 – 1.27 (m, 2H), 1.23 – 1.11 (m, 2H); ¹³C NMR (201 MHz, CDCl₃); δ (ppm): 169.54 (d, *J* = 23.5 Hz), 152.13 (s), 136.63 (s), 129.04 (s), 128.75 (s), 126.93 (s), 92.10 (d, *J* = 180.8 Hz), 83.50 (s), 64.05 (s), 40.34 (d, *J* = 20.8 Hz), 35.02 (s), 28.63 (d, *J* = 3.3 Hz), 28.53 (s), 26.07 (d, *J* = 4.3 Hz), 26.01 (s), 25.81 (s), 25.76 (s), 22.15 (s); ¹⁹F NMR (564 MHz, CDCl₃); δ (ppm): -201.83 (dd, *J* = 50.1, 26.9 Hz, 1F); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₂₀H₂₆FNO₃Na, 370.1794; found, 370.1800.

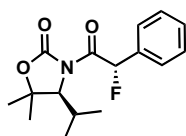


Table 3.5.3, entry 5. The title compound was prepared from oxazolidinone **3.62** (0.138 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 96:4) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 3% diethyl ether in toluene - 5% diethyl ether in toluene) to afford product as a yellow solid (0.135 g, 0.46 mmol, 92%, single diastereomer). $\alpha_D^{26} + 132.53$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.52 (d, *J* = 4.9 Hz, 2H), 7.38 (d, *J* = 5.4 Hz, 3H), 6.98 (d, *J* = 48.8 Hz, 1H), 3.99 (d, *J* = 3.1 Hz, 1H), 2.18 (dddd, *J* = 13.8, 6.9, 3.2 Hz, 1H), 1.44 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.00 (d, *J* = 6.8

Hz, 3H), 0.94 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 168.89 (d, $J = 26.9$ Hz), 152.96 (s), 133.44 (d, $J = 20.2$ Hz), 130.10 (d, $J = 3.1$ Hz), 128.77 (s), 128.76 (s), 128.49 (s), 128.46 (s), 88.87 (d, $J = 180.2$ Hz), 84.20 (s), 67.54 (s), 29.47 (s), 28.35 (s), 21.43 (s), 21.25 (s), 16.98 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -172.63 (d, $J = 48.8$ Hz, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{20}\text{FNO}_3\text{Na}$, 316.1325; found, 316.1324.

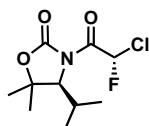


Table 3.5.3, entry 6. The title compound was prepared from oxazolidinone **3.51** (0.117 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 15% ethyl acetate in hexanes - 25% ethyl acetate in hexanes) to afford product as a white solid (84 mg, 0.34 mmol, 67%, single diastereomer). $\alpha\text{-D}^{26} + 38.40$ (c 0.7, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.45 (d, $J = 51.6$ Hz, 1H), 4.08 (d, $J = 3.0$ Hz, 1H), 2.24 – 2.18 (m, 1H), 1.56 (s, 3H), 1.45 (s, 3H), 1.09 (d, $J = 7.0$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 163.97 (d, $J = 26.3$ Hz), 152.59 (s), 90.25 (d, $J = 248.8$ Hz), 85.16 (s), 67.67 (s), 29.47 (s), 28.91 (s), 21.46 (s), 21.31 (s), 16.87 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -149.72 (dd, $J = 51.6, 3.6$ Hz, 1F);. HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{10}\text{H}_{15}\text{FCINO}_3\text{Na}$, 274.0622; found, 274.0610.

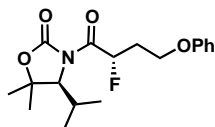


Table 3.5.3, entry 7. The title compound was prepared from oxazolidinone **3.69** (0.160 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1.5% diethyl ether in toluene) to afford product as a white solid (0.155 g, 0.46 mmol, 92%, single diastereomer). $\alpha_{\text{D}}^{26} + 31.81$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.27 (d, $J = 7.6$ Hz, 1H), 7.25 (s, 1H), 6.95 (dd, $J = 7.3$ Hz, 1H), 6.89 (d, $J = 8.3$ Hz, 2H), 6.21 (ddd, $J = 49.0, 5.3$ Hz, 1H), 4.22 – 4.14 (m, 2H), 4.13 (d, $J = 3.0$ Hz, 1H), 2.41 (ddd, $J = 5.9$ Hz, 1H), 2.37 (ddd, $J = 5.9$ Hz, 1H), 2.21 (ddd, $J = 13.8, 8.4, 5.0$ Hz, 1H), 1.53 (s, 3H), 1.41 (s, 3H), 1.08 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 169.52 (d, $J = 22.6$ Hz), 158.44 (s), 153.03 (s), 129.39 (s), 121.07 (s), 114.81 (d, $J = 0.7$ Hz), 86.32 (d, $J = 178.7$ Hz), 84.16 (s), 66.92 (s), 62.85 (d, $J = 3.3$ Hz), 32.01 (d, $J = 21.8$ Hz), 29.44 (s), 28.94 (s), 21.39 (s), 21.25 (s), 16.95 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -192.47 – -192.69 (m, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{18}\text{H}_{24}\text{FNO}_4\text{Na}$, 360.1587; found, 360.1594.

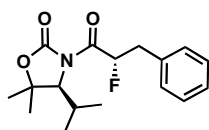


Table 3.5.3, entry 8. The title compound was prepared from oxazolidinone **3.52** (0.145 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ^1H NMR of the crude reaction mixture. The

residue was purified by column chromatography (silica, 12% ethyl acetate in hexanes - 15% ethyl acetate in hexanes) to afford product as a colorless oil after purification (0.136 g, 0.44 mmol, 88%, single diastereomer). $\alpha_D^{26} + 37.73$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.34 – 7.29 (m, 4H), 7.25 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.22 (ddd, *J* = 49.5, 8.6, 3.3 Hz, 1H), 4.10 (d, *J* = 3.0 Hz, 1H), 3.14 (dddd, *J* = 22.9, 19.4, 14.3, 6.0 Hz, 2H), 2.19 (dddd, *J* = 13.7, 6.9, 3.2 Hz, 1H), 1.51 (s, 3H), 1.30 (s, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 169.50 (d, *J* = 22.5 Hz), 152.95 (s), 135.05 (d, *J* = 1.9 Hz), 129.43 (s), 128.45 (s), 127.07 (s), 89.17 (d, *J* = 181.1 Hz), 84.00 (s), 66.73 (s), 38.47 (d, *J* = 22.5 Hz), 29.37 (s), 28.72 (s), 21.29 (s), 21.20 (s), 16.87 (s); ¹⁹F NMR (564 MHz, CDCl₃); δ (ppm): -188.75 (ddd, *J* = 49.6, 33.6, 19.4 Hz, 1F); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₇H₂₂FNO₃Na, 330.1481; found, 330.1485.

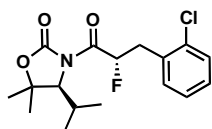


Table 3.5.3, entry 9. The title compound was prepared from oxazolidinone **3.68** (0.162 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 96:4) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 12% diethyl ether in toluene - 15% diethyl ether in toluene) to afford product as a colorless oil (0.133 g, 0.39 mmol, 78%, single diastereomer). $\alpha_D^{25} + 26.92$ (*c* 0.1, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.43 (d, *J* = 7.3 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 5.8 Hz, 1H), 7.25 – 7.18 (m, 2H), 6.32 (ddd, *J* = 48.7, 8.2, 4.2 Hz, 1H), 4.13 (d, *J* = 3.1 Hz, 1H), 3.46 (ddd, *J* = 18.6, 14.7, 8.1 Hz, 1H), 3.30 (ddd, *J* = 30.1, 14.6, 4.1 Hz, 1H), 2.21 (dddd, *J* = 13.8, 5.1 Hz, 1H), 1.53 (s, 3H),

1.35 (s, 3H), 1.07 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 169.34 (d, $J = 22.6$ Hz), 152.78 (s), 134.54 (s), 132.75 (d, $J = 2.9$ Hz), 131.58 (d, $J = 1.3$ Hz), 129.55 (s), 128.61 (s), 126.93 (s), 87.69 (d, $J = 181.0$ Hz), 83.95 (s), 66.88 (s), 35.20 (d, $J = 22.7$ Hz), 29.52 (s), 28.90 (s), 21.49 (s), 21.33 (s), 16.96 (s). ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -187.68, -187.87 (m, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{21}\text{FCINO}_3\text{Na}$, 364.109; found, 364.1102.

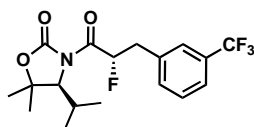


Table 3.5.3, entry 10. The title compound was prepared from oxazolidinone **3.60** (0.179 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1.5% diethyl ether in toluene) to afford product as a white solid (0.115 g, 0.31 mmol, 61%, 98:2 dr. $\alpha_{\text{D}}^{26} + 25.27$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.57 (s, 1H), 7.56 – 7.51 (m, 2H), 7.45 (dd, $J = 7.7$ Hz, 1H), 6.18 (ddd, $J = 49.4, 8.7, 2.5$ Hz, 1H), 4.12 (d, $J = 2.9$ Hz, 1H), 3.19 (dddd, $J = 34.6, 23.1, 14.5, 5.7$ Hz, 2H), 2.21 (dddd, $J = 13.7, 6.9, 3.2$ Hz, 1H), 1.54 (s, 3H), 1.35 (s, 3H), 1.07 (d, $J = 7.0$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 169.15 (d, $J = 22.5$ Hz), 153.11 (s), 136.24 (d, $J = 1.0$ Hz), 133.00 (s), 130.88 (q, $J = 32.2$ Hz), 129.03 (s), 126.26 (q, $J = 3.7$ Hz), 124.12 (q, $J = 3.8$ Hz), 124.01 (d, $J = 273.42$ Hz), 89.08 (d, $J = 181.9$ Hz), 84.29 (s), 66.87 (s), 38.23 (d, $J = 22.5$ Hz), 29.48 (s), 28.91 (s), 21.38 (s), 21.27 (s), 16.95 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -62.65 (s, 3F), -189.13

(ddd, $J = 49.5, 34.0, 20.1$ Hz, 1F); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{18}H_{21}F_4NO_3Na$, 398.1355; found, 398.1356.

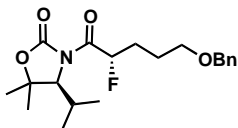


Table 3.5.3, entry 11. The title compound was prepared from oxazolidinone **3.57** (0.174 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by 1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 15% ethyl acetate in hexanes hexanes – 25% ethyl acetate in hexanes) to afford product as a colorless oil (0.124 g, 0.34 mmol, 68%, single diastereomer). $\alpha_D^{25} + 30.86$ (c 1.0, $CHCl_3$); 1H NMR (600 MHz, $CDCl_3$); δ (ppm): 7.35 – 7.30 (m, 4H), 7.29 – 7.26 (m, 1H), 6.10 – 5.99 (m, 1H), 4.49 (d, $J = 2.8$ Hz, 2H), 4.10 (d, $J = 3.0$ Hz, 1H), 3.57 – 3.49 (m, 2H), 2.20 (dddd, $J = 13.9, 7.0, 3.2$ Hz, 1H), 2.02 – 1.91 (m, 2H), 1.90 – 1.79 (m, 2H), 1.53 (s, 3H), 1.36 (s, 3H), 1.07 (d, $J = 7.0$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (201 MHz, $CDCl_3$); δ (ppm): 171.99 (d, $J = 22.7$ Hz), 154.85 (s), 140.20 (s), 130.11 (s), 129.43 (s), 129.29 (s), 90.71 (d, $J = 178.8$ Hz), 85.87 (s), 74.58 (s), 70.99 (s), 68.68 (s), 31.26 (s), 31.01 (d, $J = 22.1$ Hz), 30.71 (s), 26.80 (d, $J = 2.0$ Hz), 23.18 (s), 23.10 (s), 18.76 (s); ^{19}F NMR (564 MHz, $CDCl_3$); δ (ppm): -192.32 (ddd, $J = 50.1, 30.1, 24.4$ Hz, 1F). HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{20}H_{28}FNO_4Na$, 388.1900; found, 388.1901.

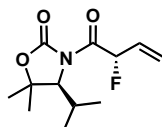


Table 3.5.3, entry 12. The title compound was prepared from oxazolidinone **3.61** (0.113 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr >98:2) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 15% ethyl acetate in hexanes - 25% ethyl acetate in hexanes) to afford product as a clear oil (56 mg, 0.23 mmol, 46%, single diastereomer). $\alpha_{\text{D}}^{25} + 36.44$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); δ (ppm): 6.46 (dd, $J = 48.7, 6.2$ Hz, 1H), 6.07 – 5.97 (m, 1H), 5.65 (dd, $J = 17.3, 3.2$ Hz, 1H), 5.46 (d, $J = 10.7$ Hz, 1H), 4.07 (d, $J = 2.9$ Hz, 1H), 2.19 (dddd, $J = 13.7, 6.9, 3.1$ Hz, 1H), 2.19 (dddd, $J = 13.7, 6.9, 3.1$ Hz, 1H), 1.52 (s, 3H), 1.34 (s, 3H), 1.08 (d, $J = 7.0$ Hz, 3H), 0.98 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); δ (ppm): 168.36 (d, $J = 24.7$ Hz), 153.03 (s), 129.94 (d, $J = 19.8$ Hz), 121.75 (d, $J = 10.9$ Hz), 87.69 (d, $J = 179.0$ Hz), 84.32 (s), 67.19 (s), 29.46 (s), 28.96 (s), 21.33 (s), 16.94 (s); ^{19}F NMR (564 MHz, CDCl_3); δ (ppm): -186.01 (ddd, $J = 49.0, 14.3, 3.6$ Hz, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{18}\text{FNO}_3\text{Na}$, 266.1168; Found, 266.1158.

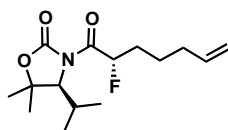


Table 3.5.3, entry 13. The title compound was prepared from oxazolidinone **3.56** (0.134 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 98:2) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 9% ethyl acetate in hexanes - 11%

ethyl acetate in hexanes) to afford product as a colorless oil (0.114 g, 0.40 mmol, 80%, single diastereomer). $\alpha_D^{26} + 31.46$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 6.05 – 5.94 (m, 1H), 5.78 (dddd, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.99 (dd, *J* = 32.4, 13.7 Hz, 2H), 4.10 (d, *J* = 2.9 Hz, 1H), 2.19 (dddd, *J* = 10.3, 7.2, 3.3 Hz, 1H), 2.16 – 2.05 (m, 2H), 1.88 – 1.77 (m, 2H), 1.70 – 1.60 (m, 2H), 1.53 (s, 3H), 1.38 (s, 3H), 1.07 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 170.32 (d, *J* = 22.6 Hz), 153.05 (s), 137.78 (s), 115.14 (s), 89.00 (d, *J* = 178.7 Hz), 84.04 (s), 66.86 (s), 32.95 (s), 31.72 (d, *J* = 22.1 Hz), 29.45 (s), 28.94 (s), 24.01 (d, *J* = 1.9 Hz), 21.37 (s), 21.29 (s), 16.95 (s); ¹⁹F NMR (564 MHz, CDCl₃); δ (ppm): -192.17 – -192.40 (m, 1F); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₅H₂₄FNO₃Na, 308.1638; found, 308.1642.

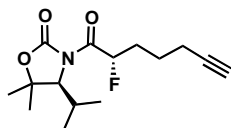


Table 3.5.3, entry 3.58. The title compound was prepared from oxazolidinone **S12** (0.132 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 5:1) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 12% ethyl acetate in hexanes) to afford product as a colorless oil (79 mg, 0.28 mmol, 56%, single diastereomer). $\alpha_D^{26} + 30.73$ (*c* 0.316, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ (ppm): 6.02 (ddd, *J* = 50.1, 7.4, 3.6 Hz, 1H), 4.11 (d, *J* = 2.8 Hz, 1H), 2.28 (dt, *J* = 16.7, 8.0 Hz, 2H), 2.24 – 2.18 (m, 1H), 2.06 – 1.89 (m, 3H), 1.78 (ddd, *J* = 22.5, 14.4, 7.0 Hz, 2H), 1.54 (s, 3H), 1.40 (s, 3H), 1.08 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 2H); ¹³C NMR (201 MHz, CDCl₃) δ (ppm): 170.04 (d, *J* = 22.6 Hz), 153.06 (s), 88.76 (d, *J* = 179.1 Hz), 84.12 (s), 83.36 (s), 69.02 (s), 66.91 (s), 31.27

(d, $J = 22.1$ Hz), 29.48 (s), 29.02 (s), 23.77 (d, $J = 2.0$ Hz), 21.41 (s), 21.31 (s), 17.99 (s), 16.98 (s). ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -192.21 (ddd, $J = 50.0, 31.2, 23.3$ Hz). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{22}\text{FNO}_3\text{Na}$, 306.1481; found, 306.1476.

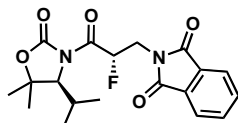
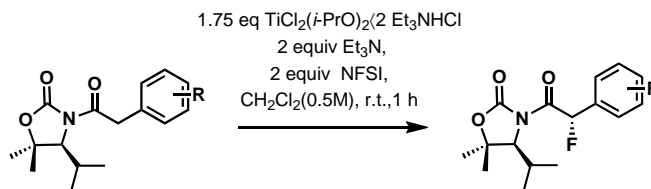


Table 3.5.3, entry 15. The title compound was prepared from oxazolidinone **3.59** (0.179 g, 0.50 mmol) following the standard α -monofluorination procedure. The diastereoselectivity (dr 94:6) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 5% diethyl ether in toluene - 10% diethyl ether in toluene) to afford product as a white solid (0.132 g, 0.35 mmol, 70%, single diastereomer). $\alpha_{\text{D}}^{22} + 13.20$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.75 (ddd, $J = 72.2, 5.3, 3.1$ Hz, 4H), 6.22 (ddd, $J = 46.7, 4.4, 1.9$ Hz, 1H), 4.38 (ddd, $J = 15.3, 10.7, 4.7$ Hz, 1H), 4.26 (ddd, $J = 31.6, 15.2, 1.6$ Hz, 1H), 4.16 (d, $J = 2.8$ Hz, 1H), 2.19 (dddd, $J = 6.8, 3.9$ Hz, 1H), 1.69 (s, 3H), 1.55 (s, 3H), 1.01 (d, $J = 7.0$ Hz, 3H), 0.95 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 167.74 (s), 167.51 (d, $J = 23.2$ Hz), 153.48 (s), 134.07 (s), 131.73 (s), 123.47 (s), 85.87 (d, $J = 183.8$ Hz), 84.73 (s), 66.68 (s), 38.08 (d, $J = 21.7$ Hz), 29.43 (s), 28.83 (s), 21.84 (s), 21.16 (s), 17.01 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -194.15 (ddd, $J = 44.1, 32.2, 11.3$ Hz, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{21}\text{FN}_2\text{O}_5\text{Na}$, 399.1332; found, 399.1339.

Standard procedure for α -monofluorination of *N*-(arylacetyl)oxazolidinones:



Preparation of $\text{TiCl}_2(i\text{PrO})_2 \cdot 2 \text{Et}_3\text{NHCl}$: In a flame dried flask, *i*-PrOH (2 equiv) was added to TiCl_4 (1 equiv, 1.0 M in CH_2Cl_2) dropwise over 5 min at rt under an argon. The mixture was stirred for an additional 10 min (HCl gas evolution was observed). Et_3N (2 equiv) was then added dropwise over 10 min at rt. The mixture was stirred for an additional 30 min (most of the initially formed white precipitate eventually redissolves).

α -Monofluorination reaction: In a separate flame-dried flask, $\text{TiCl}_2(i\text{PrO})_2 \cdot 2\text{Et}_3\text{NHCl}$ (1.75 equiv) was added dropwise to the solution of *N*-acyl oxazolidinone (0.50 mmol, 1.00 equiv) in CH_2Cl_2 (0.5 M) at 0 °C under argon, and the resultant mixture was stirred for 5 min (solution becomes a deep red upon complete addition). Et_3N (2.0 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 30 min. NFSI (2.0 equiv) was added in one portion to the reaction at 0 °C (CAUTION: reaction mixture may bubble vigorously upon addition of NFSI). The reaction mixture was warmed to rt and stirred for 1 h. The reaction was filtered through a 1.5 cm silica gel plug and washed with dichloromethane (10 mL) and ethyl acetate (50 mL). The filtrate was then concentrated and the residue was purified by flash column chromatography to give the product.

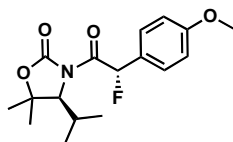


Table 3.5.5, entry 1. The title compound was prepared from oxazolidinone **3.53** (0.153 g, 0.50 mmol) following the standard α -monofluorination of *N*-(arylacetyl)oxazolidinones. The diastereoselectivity (dr 93:7) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 4% diethyl ether in toluene) to afford product as a colorless oil (0.102 g, 0.31 mmol, 63%, single diastereomer). $\alpha_D^{26} + 141.92$ (*c* 0.3, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.45 (d, $J = 8.3$ Hz, 2H), 6.91 (d, $J = 48$ Hz, 1 H), 6.89 (d, $J = 8.5$ Hz, 2H), 4.01 (d, $J = 3.0$ Hz, 1H), 3.81 (s, 3H), 2.18 (dddd, $J = 13.8, 6.9, 3.2$ Hz, 1H), 1.57 (s, 3H), 1.45 (s, 3H), 1.12 (d, $J = 7.1$ Hz, 3H), 1.00 (d, $J = 6.8$ Hz, 3H), 0.98 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 169.14 (d, $J = 27.8$ Hz), 160.89 (d, $J = 2.9$ Hz), 152.94 (s), 130.25 (s), 130.22 (s), 125.55 (d, $J = 21.0$ Hz), 114.15 (s), 114.14 (s), 88.60 (d, $J = 179.9$ Hz), 84.14 (s), 67.45 (s), 55.29 (s), 29.50 (s), 28.49 (s), 21.45 (s), 21.28 (s), 17.01 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -169.50 (d, $J = 49.4$ Hz, 1F). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{22}\text{FNO}_4\text{Na}$, 346.1431; found, 346.1439.

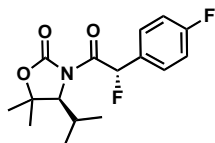


Table 3.5.5, entry 2. The title compound was prepared from oxazolidinone **3.54** (0.146 g, 0.50 mmol) following the standard procedure for α -monofluorination of *N*-(arylacetyl)oxazolidinones. The diastereoselectivity (dr 10:1) was determined by ^1H NMR of

the crude reaction mixture. The residue was purified by column chromatography (silica, 1% diethyl ether in toluene) to afford product as a white solid (0.110 g, 0.36 mmol, 71%, single diastereomer). $\alpha_D^{25} + 141.77$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.53 – 7.49 (m, 1H), 7.06 (dd, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 48.6 Hz, 1H), 3.99 (d, *J* = 2.9 Hz, 1H), 2.17 (ddd, *J* = 10.5, 6.8, 3.3 Hz, 1H), 1.44 (s, 2H), 1.10 (d, *J* = 7.0 Hz, 2H), 0.98 (d, *J* = 6.8 Hz, 1H), 0.97 (s, 1H); ¹³C NMR (126 MHz, CDCl₃); δ (ppm): 168.66 (d, *J* = 27.2 Hz), 163.58 (dd, *J* = 250.0, 3.2 Hz), 152.90 (s), 130.65 (d, *J* = 4.3 Hz), 130.59 (d, *J* = 4.3 Hz), 129.45 (dd, *J* = 20.9, 3.3 Hz), 115.91 (d, *J* = 1.7 Hz), 115.73 (d, *J* = 1.7 Hz), 88.00 (d, *J* = 180.5 Hz), 84.26 (s), 67.44 (s), 29.43 (s), 28.40 (s), 21.39 (s), 21.16 (s), 16.90 (s); ¹⁹F NMR (564 MHz, CDCl₃); δ (ppm): -110.25 – -110.31 (m, 1F), -171.32 (dd, *J* = 48.6, 5.4 Hz, 1F); HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₆H₁₉F₂NO₃Na, 334.1234; found, 334.1240.

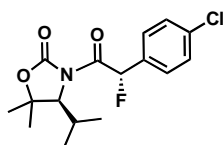


Table 3.5.5, entry 3. The title compound was prepared from oxazolidinone **3.63** (0.155 g, 0.50 mmol) following the standard procedure for α -monofluorination of *N*-(arylacetyl)oxazolidinones. The diastereoselectivity (dr 10:1) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 3% diethyl ether in toluene – 5% diethyl ether in toluene) to afford product as green crystals (0.100 g, 0.31 mmol, 61%, 10:1 dr, single diastereomer). $\alpha_D^{26} + 125.38$ (*c* 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃); δ (ppm): 7.47 (d, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 6.95 (d, *J* = 48.5 Hz, 1H), 4.00 (d, *J* = 2.7 Hz, 1H), 2.21 – 2.15 (m, 1H), 1.45 (s, 3H), 1.11 (d, *J* =

7.0 Hz, 3H), 1.00 (s, 4H), 0.99 (s, 1H); ^{13}C NMR (151 MHz, CDCl_3); $\delta(\text{ppm})$: 168.46 (d, $J = 26.9$ Hz), 152.91 (s), 136.21 (d, $J = 3.5$ Hz), 131.95 (d, $J = 20.6$ Hz), 129.89 (s), 129.86 (s), 129.05 (s), 129.04 (s), 88.02 (d, $J = 180.6$ Hz), 84.33 (s), 67.45 (s), 29.46 (s), 28.54 (s), 21.42 (s), 21.22 (s), 16.94 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -172.51 (d, $J = 48.5$ Hz, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{19}\text{FNO}_3\text{Na}$, 350.0935; found, 350.0928.

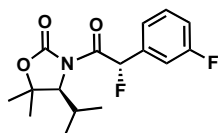


Table 3.5.5, entry 4. The title compound was prepared from oxazolidinone **3.66** (0.147 g, 0.50 mmol) following the standard procedure for α -monofluorination of *N*-(arylacetyl)oxazolidinones. The diastereoselectivity (dr 93:7) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1% diethyl ether in toluene) to afford product as a white solid (0.107 g, 0.35 mmol, 69%, single diastereomer). $\alpha\text{D}_D^{26} + 126.11$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.38 – 7.29 (m, 2H), 7.26 – 7.22 (m, 1H), 7.08 (dddd, $J = 9.6, 5.6, 1.4$ Hz, 1H), 6.98 (d, $J = 48.5$ Hz, 1H), 3.99 (d, $J = 3.2$ Hz, 1H), 2.18 (dddd, $J = 13.9, 6.9, 3.2$ Hz, 1H), 1.45 (s, 3H), 1.10 (d, $J = 7.0$ Hz, 3H), 1.02 – 0.97 (m, 6H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 168.34 (d, $J = 26.6$ Hz), 162.64 (dd, $J = 247.8, 1.5$ Hz), 152.97 (s), 135.72 (dd, $J = 20.6, 7.4$ Hz), 130.44 (dd, $J = 8.1, 1.4$ Hz), 124.13 (dd, $J = 4.8, 3.2$ Hz), 117.17 (dd, $J = 21.1, 2.8$ Hz), 115.34 (dd, $J = 22.7, 4.8$ Hz), 87.95 (dd, $J = 181.1, 1.8$ Hz), 84.37 (s), 67.54 (s), 29.48 (s), 28.46 (s), 21.43 (s), 21.24 (s), 16.95 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -111.55 (td, $J = 9.6, 6.0$

Hz, 1F), -173.59 (d, $J = 48.9$ Hz); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{16}H_{19}F_2NO_3Na$; 334.1231; found, 334.1241.

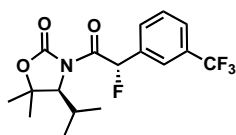


Table 3.5.5, entry 5. The title compound was prepared from oxazolidinone **3.71** (0.172 g, 0.50 mmol) following the standard procedure for α -monofluorination of N -(arylacetyl)oxazolidinones. The diastereoselectivity (dr 10:1) was determined by 1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1% diethyl ether in toluene) to afford product as a white solid (0.117 g, 0.33 mmol, 65%, 10:1 dr, single diastereomer). $\alpha_D^{26} + 140.82$ (c 0.8, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.79 – 7.72 (m, 2H), 7.67 (d, $J = 7.4$ Hz, 1H), 7.54 (dd, $J = 7.8$ Hz, 1H), 7.04 (d, $J = 48.5$ Hz, 1H), 4.03 (d, $J = 3.2$ Hz, 1H), 2.20 (dddd, $J = 13.9, 6.9, 3.2$ Hz, 1H), 1.46 (s, 3H), 1.12 (d, $J = 7.0$ Hz, 3H), 1.01 (d, $J = 7.7$ Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 168.17 (d, $J = 26.4$ Hz), 152.93 (s), 134.56 (d, $J = 20.6$ Hz), 132.21 (dd, $J = 4.5, 1.1$ Hz), 131.80 – 130.88 (m), 129.40 (d, $J = 1.2$ Hz), 126.96 – 126.64 (m), 125.02 – 124.76 (m), 123.60 (d, $J = 272.5$ Hz), 88.06 (d, $J = 181.2$ Hz), 84.45 (s), 67.50 (s), 29.50 (s), 28.43 (s), 21.43 (s), 21.25 (s), 16.97 (s); ^{19}F NMR (564 MHz, $CDCl_3$); δ (ppm): -62.85 (s, 3F), -173.31 (d, $J = 48.5$ Hz, 1F); HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{17}H_{19}F_4NO_3Na$, 384.1199; found, 384.1196.

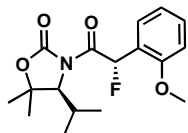


Table 3.5.5, entry 6. The title compound was prepared from oxazolidinone **3.70** (0.153 g, 0.50 mmol) following the standard procedure for α -monofluorination of *N*-(arylacetyl)oxazolidinones. The diastereoselectivity (dr 10:1) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1.5% diethyl ether in toluene – 3% diethyl ether in toluene) to afford product as a colorless oil (0.129 g, 0.40 mmol, 80%, single diastereomer. $\alpha_D^{26} + 158.73$ (c 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.35 (dd, $J = 7.8$ Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.22 (d, $J = 48.5$ Hz, 1H), 6.94 (dd, $J = 14.7, 7.7$ Hz, 2H), 4.11 (d, $J = 3.0$ Hz, 1H), 3.86 (s, 3H), 2.20 (dddd, $J = 13.7, 6.9, 2.9$ Hz, 1H), 1.46 (s, 3H), 1.21 (s, 3H), 1.11 (d, $J = 7.0$ Hz, 3H), 0.99 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 168.90 (d, $J = 25.6$ Hz), 157.66 (d, $J = 3.7$ Hz), 152.55 (s), 131.39 (d, $J = 3.4$ Hz), 128.11 (d, $J = 5.0$ Hz), 122.39 (d, $J = 19.1$ Hz), 120.54 (d, $J = 1.2$ Hz), 111.38 (s), 84.82 (d, $J = 177.7$ Hz), 83.84 (s), 67.14 (s), 55.80 (s), 29.51 (s), 28.57 (s), 21.40 (s), 21.32 (s), 16.88 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -177.76 (d, $J = 48.4$ Hz, 1F); HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{22}\text{FNO}_4\text{Na}$, 346.1431; found, 346.1436.

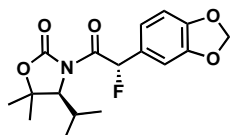


Table 3.5.5, entry 7. The title compound was prepared from oxazolidinone **3.64** (0.160 g, 0.50 mmol) following the standard procedure for α -monofluorination of *N*-

(arylacetyl)oxazolidinones. The diastereoselectivity (dr 10:1) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1.5% diethyl ether in toluene – 2% diethyl ether in toluene) to afford product as a white solid (0.107 g, 0.32 mmol, 64%, single diastereomer). $\alpha_{\text{D}}^{26} + 138.76$ (c 0.83, CHCl_3); ^1H NMR (600 MHz, CDCl_3); $\delta(\text{ppm})$: 7.01 (d, $J = 9.2$ Hz, 2H), 6.88 (d, $J = 48.7$ Hz, 1H), 6.80 (d, $J = 7.8$ Hz, 1H), 5.98 (s, 2H), 4.01 (d, $J = 3.1$ Hz, 1H), 2.21 – 2.15 (m, 1H), 1.47 (s, 3H), 1.12 (d, $J = 7.0$ Hz, 3H), 1.05 (s, 3H), 1.00 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (201 MHz, CDCl_3); $\delta(\text{ppm})$: 206.97 (s), 168.90 (d, $J = 27.8$ Hz), 152.94 (s), 148.52 (dd, $J = 224.9, 2.4$ Hz), 127.10 (d, $J = 20.9$ Hz), 123.07 (d, $J = 5.2$ Hz), 108.63 (dd, $J = 89.3, 2.9$ Hz), 101.46 (s), 88.54 (d, $J = 180.6$ Hz), 84.21 (s), 67.47 (s), 30.92 (s), 29.50 (s), 28.59 (s), 21.45 (s), 21.29 (s), 17.00 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -169.32 – -169.84 (m, 1F). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{20}\text{FNO}_5\text{Na}$ 360.1223; found, 360.1226

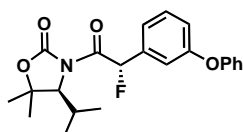


Table 3.5.5, entry 8. The title compound was prepared from oxazolidinone **3.65** (0.184 g, 0.50 mmol) following the standard procedure for α -monofluorination of N -(arylacetyl)oxazolidinones. The diastereoselectivity (dr 95:5) was determined by ^1H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 1% diethyl ether in toluene) to afford product as a white solid (0.119 g, 0.31 mmol, 62%, single diastereomer). $\alpha_{\text{D}}^{26} + 148.96$ (c 1.0, CHCl_3); ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.31 – 7.26 (m, 3H), 7.19 (d, $J = 7.9$ Hz, 1H), 7.13 (s, 1H), 7.05 (dd, $J = 7.4$ Hz, 1H), 6.97 (d, $J =$

8.1 Hz, 1H), 6.93 (s, 1H), 6.91 (d, $J = 7.9$ Hz, 2H), 6.83 (s, 1H), 3.94 (d, $J = 3.0$ Hz, 1H), 2.13 (dddd, $J = 13.8, 6.9, 3.1$ Hz, 1H), 1.40 (s, 3H), 1.05 (d, $J = 7.0$ Hz, 3H), 0.97 (s, 3H), 0.94 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3); $\delta(\text{ppm})$: 168.53 (d, $J = 26.7$ Hz), 157.57 (d, $J = 1.6$ Hz), 156.66 (s), 152.91 (s), 135.24 (d, $J = 20.3$ Hz), 130.17 (d, $J = 1.6$ Hz), 129.83 (s), 123.65 (s), 123.16 (d, $J = 4.6$ Hz), 120.38 (d, $J = 3.0$ Hz), 118.96 (s), 118.79 (d, $J = 4.6$ Hz), 88.50 (d, $J = 180.8$ Hz), 84.28 (s), 67.51 (s), 29.50 (s), 28.54 (s), 21.43 (s), 21.28 (s), 16.99 (s); ^{19}F NMR (564 MHz, CDCl_3); $\delta(\text{ppm})$: -172.83 (d, $J = 48.8$ Hz, 1F). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{24}\text{FNO}_4\text{Na}$, 408.1587; found, 408.1600

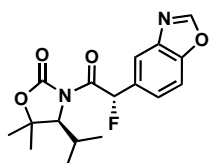


Table 3.5.5, entry 9

Preparation of $\text{TiCl}_2(i\text{PrO})_2 \cdot 2 \text{Et}_3\text{NHCl}$: In a flame dried flask under argon, $i\text{PrOH}$ (2 equiv) was added dropwise to TiCl_4 (1 equiv, 1.0 M in CH_2Cl_2) over 5 min at rt. The mixture was stirred for an additional 10 min (HCl gas evolution was observed). Et_3N (2 equiv) was then added dropwise over 10 min at rt. The mixture was stirred for an additional 30 min (white precipitate initially forms but majority eventually redissolves into solution).

α -Monofluorination reaction: In a separate flame dried flask under argon $\text{TiCl}_2(i\text{PrO})_2 \cdot 2\text{Et}_3\text{NHCl}$ (0.33 mL, ca. 1.0 M solution in CH_2Cl_2 , 1.75 equiv) was added dropwise to the solution of N -acyl oxazolidinone **3.73** (0.10 g, 0.31 mmol, 1.00 equiv) in CH_2Cl_2 (0.38 mL) at 0 °C and stirred for 3 min (solution should become a deep red upon complete addition). Et_3N (86 μL , 0.62 mmol, 2.0 equiv) was added dropwise to the reaction

mixture at 0 °C and stirred for 3 min. NFSI (0.195 g, 0.62 mmol, 2.0 equiv) was added in one portion to the reaction at 0 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was filtered through a 1.5 cm silica gel plug and washed with dichloromethane (10 mL) and ethyl acetate (60 mL). The filtrate was then concentrated *in vacuo*. The diastereoselectivity (dr 92:8) was determined by ¹H NMR of the crude reaction mixture. The residue was purified by column chromatography (silica, 4% diethyl ether in toluene) to afford product as a white solid (0.119 g, 0.31 mmol, 87%, mixture of diastereomers). $\alpha_D^{21} + 115.77$ (c 1.0, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ (ppm): 8.13 (s, 1H), 7.98 (s, 1H), 7.61 (s, 2H), 7.10 (d, *J* = 48.6 Hz, 1H), 4.03 (d, *J* = 2.9 Hz, 1H), 2.25 – 2.15 (m, 1H), 1.44 (s, 3H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.95 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ (ppm): 168.69 (d, *J* = 27.1 Hz), 153.42 (s), 152.87 (s), 150.88 – 150.72 (m), 140.35 (s), 130.35 (d, *J* = 20.8 Hz), 126.45 (d, *J* = 4.2 Hz), 121.22 (d, *J* = 4.6 Hz), 111.40 (d, *J* = 1.5 Hz), 88.62 (d, *J* = 180.9 Hz), 84.25 (s), 67.42 (s), 29.50 (s), 28.59 (s), 21.44 (s), 21.24 (s), 16.98 (s). ¹⁹F NMR (564 MHz, CDCl₃) δ (ppm): -169.22 (s), -169.31 (s). HRMS-ESI (*m/z*): [M+Na]⁺ calcd for C₁₇H₁₉FN₂O₄Na, 357.1227; found, 357.1224.

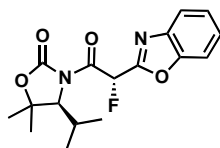


Table 3.5.5, entry 10.

Preparation of TiCl₂(OPr-*i*)₂: In a flame-dried flask, Ti(OPr-*i*)₄ (1.0 equiv) was added dropwise to TiCl₄ (1.0 equiv, 1.0 M in CH₂Cl₂) over 5 min at rt under argon. The mixture was stirred for an additional 10 min.

α -Monofluorination reaction: In a separate flame-dried flask, $\text{TiCl}_2(\text{OPr-}i)_2$ (0.44 mL, ca. 2.0 M solution in CH_2Cl_2 , 1.75 equiv) was added dropwise to the solution of *N*-acyl oxazolidinone **3.74** (0.158 g, 0.50 mmol, 1.00 equiv) in CH_2Cl_2 (0.38 mL) at 0 °C and stirred for 2 min under argon. Et_3N (0.14 mL, 1.0 mmol, 2.0 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 2 min. NFSI (0.315 g, 1.0 mmol, 2.0 equiv) was added in one portion to the reaction at 0 °C. The reaction mixture was warmed to rt and stirred for 30 min. The reaction was filtered through a 1.5 cm silica gel plug and washed with dichloromethane (10 mL) and ethyl acetate (60 mL). The filtrate was then concentrated *in vacuo*. The diastereoselectivity (dr 2:1) was determined by ^1H NMR analysis of the crude product. The residue was purified by column chromatography (silica, 4% diethyl ether in toluene) to afford product as a white solid (0.105 g, 0.32 mmol, 63%, single diastereomer).

$\alpha\text{D}^{21}_D + 77.97$ (*c* 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.68 (d, $J = 7.9$ Hz, 1H), 7.60 (d, $J = 8.2$ Hz, 1H), 7.42 (t, $J = 7.8$ Hz, 1H), 7.36 (t, $J = 7.7$ Hz, 1H), 7.06 (d, $J = 50.4$ Hz, 1H), 4.30 (d, $J = 3.0$ Hz, 1H), 2.24 (dq, $J = 6.8, 3.8$ Hz, 1H), 1.59 (s, 3H), 1.53 (s, 3H), 1.15 (d, $J = 7.0$ Hz, 3H), 1.02 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ (ppm): 164.15 (d, $J = 23.3$ Hz), 158.11 (d, $J = 21.8$ Hz), 153.66 (s), 151.09 (s), 126.53 (d, $J = 1.2$ Hz), 124.96 (s), 120.82 (d, $J = 0.9$ Hz), 111.34 (d, $J = 0.9$ Hz), 85.65 (s), 82.90 (d, $J = 183.5$ Hz), 67.34 (s), 29.56 (s), 28.81 (s), 21.59 (s), 21.43 (s), 16.99 (s). ^{19}F NMR (564 MHz, CDCl_3) δ (ppm): -185.48 (s), -185.57 (s). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{19}\text{FN}_2\text{O}_4\text{Na}$, 357.1227; found, 357.1216.

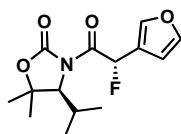
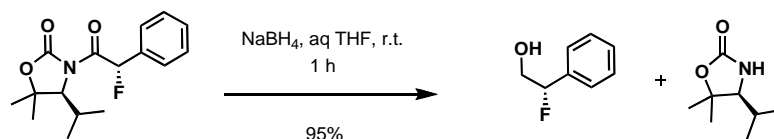


Table 3.5.5, entry 8.

Preparation of $\text{TiCl}_2(\text{OPr-}i)_2 \cdot 2 \text{Et}_3\text{NHCl}$: In a flame dried-flask, *i*-PrOH (2 equiv) was added dropwise to TiCl_4 (1 equiv, 1.0 M in CH_2Cl_2) over 5 min at rt under argon. The mixture was stirred for an additional 10 min (HCl gas evolution was observed). Et_3N (2 equiv) was then added dropwise over 10 min at rt. The mixture was stirred for an additional 30 min (white precipitate initially forms but eventually redissolves).

α -Monofluorination reaction: In a separate flame-dried flask, $\text{TiCl}_2(\text{OPr-}i)_2 \cdot 2\text{Et}_3\text{NHCl}$ (0.33 mL, ca. 1.0 M solution in CH_2Cl_2 , 1.75 equiv) was added dropwise to the solution of *N*-acyl oxazolidinone **3.67** (50 mg, 0.19 mmol, 1.00 equiv) in CH_2Cl_2 (0.38 mL) at 0 °C under argon, and the resulting mixture was stirred for 2 min (solution should become a deep red upon complete addition). Et_3N (53 μL , 0.38 mmol, 2.0 equiv) was added dropwise at 0 °C and the reaction mixture was stirred for 2 min. NFSI (0.12 g, 0.38 mmol, 2.0 equiv) was added in one portion to the reaction at 0 °C. The reaction mixture was warmed to rt and stirred for 30 min. The reaction was filtered through a 1.5 cm silica gel plug and washed with dichloromethane (10 mL) and ethyl acetate (60 mL). The filtrate was then concentrated *in vacuo*. The diastereoselectivity (10:1) was determined by ^1H NMR analysis of the crude mixture of products. The residue was purified by column chromatography (silica, 4% diethyl ether in toluene) to afford product as a white solid (29 mg, 0.103 mmol, 54%, single diastereomer). $\alpha_{\text{D}}^{20} + 61.94$ (*c* 1.0, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ (ppm): 7.65 (d, *J* = 4.0 Hz, 1H), 7.41 (d, *J* = 1.1 Hz, 1H), 6.99 (d, *J* = 48.6 Hz, 1H), 6.52 (s, 1H), 4.02 (d, *J* =

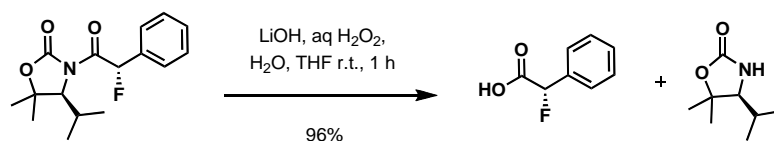
2.5 Hz, 1H), 2.22 – 2.13 (m, 1H), 1.48 (s, 3H), 1.10 (d, $J = 5.8$ Hz, 6H), 1.00 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) $\delta(\text{ppm})$: 168.55 (d, $J = 27.2$ Hz), 153.03 (s), 143.80 (d, $J = 7.4$ Hz), 143.29 (d, $J = 8.7$ Hz), 118.94 (d, $J = 24.2$ Hz), 108.79 (s), 84.31 (s), 82.04 (dd, $J = 177.6, 10.1$ Hz), 67.30 (d, $J = 12.0$ Hz), 29.50 (s), 28.58 (s), 21.44 (s), 21.26 (d, $J = 2.7$ Hz), 16.96 (d, $J = 4.1$ Hz). ^{19}F NMR (564 MHz, CDCl_3) $\delta(\text{ppm})$: -176.65 (d, $J = 4.8$ Hz), -176.73 (d, $J = 4.8$ Hz). HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{18}\text{FNO}_4\text{Na}$, 306.1118; found, 306.1122.



(S)-2-Fluoro-2-phenylethanol. Sodium borohydride (63.7 mg, 1.68 mmol) was added to a solution of the substrate (0.175 g, 0.561 mmol) in a 3:1 mixture of THF:H₂O (8.50 mL) at 0 °C and the reaction mixture was stirred for 10 min. The reaction mixture was warmed to rt and stirred an additional 1 h. The reaction mixture was quenched with aqueous 1 M HCl (5 mL). The layers were separated. The aqueous layer was extracted with diethyl ether (3 x 5 mL). The organic layers were combined and washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and the residue purified by column chromatography (silica, 50% diethyl ether in pentane - 80% diethyl ether in pentane) to afford the desired alcohol (72.2 mg, 0.52 mmol, 93%) and the purified oxazolidinone (83 mg, 0.53 mmol, 95%). $\alpha_{\text{D}}^{23} + 51.03$ (c 1.0, CHCl_3). ^1H NMR (600 MHz, CDCl_3) $\delta(\text{ppm})$: 7.38 (dt, $J = 17.5, 7.3$ Hz, 5H), 5.57 (ddd, $J = 48.7, 7.8, 2.8$ Hz, 1H), 3.98 – 3.89 (m, 1H), 3.83 (dd, $J = 30.1, 12.5$ Hz, 1H), 2.38 (s, 1H). ^{13}C NMR (126 MHz, CDCl_3) $\delta(\text{ppm})$: 136.34 (d, $J = 19.6$ Hz), 128.74 (d, $J = 1.7$

Hz), 128.54 (s), 125.68 (d, $J = 7.0$ Hz), 94.80 (d, $J = 171.9$ Hz), 66.48 (d, $J = 24.7$ Hz). ^{19}F NMR (564 MHz, CDCl_3) $\delta(\text{ppm})$: -186.89 (ddd, $J = 49.5, 30.6, 19.1$ Hz). HRMS-EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_8\text{H}_9\text{FO}$, 140.0637; found, 140.0634.

Determination of er for the product: 2-Naphthoyl chloride (3.0 equiv.) was added to a solution of the purified alcohol, triethylamine (3.0 equiv.), and 4-dimethylaminopyridine (0.5 equiv.) in dichloromethane (0.1 M) at 0 °C. After 10 min, the reaction was warmed to rt and stirred for 30 min. The reaction was quenched with aqueous ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and purified by column chromatography (silica, 15% ethyl acetate in hexanes) to afford the desired naphthoyl ester derivative. HPLC analysis of the 2-naphthoyl ester derivative (OJ-H, 2.5% *i*PrOH - hexanes, 1.0 mL/min, 254 nm) indicated er of 0.8:99.2: R_T (minor) = 37.5 minutes, R_T (major) = 45.5 minutes.



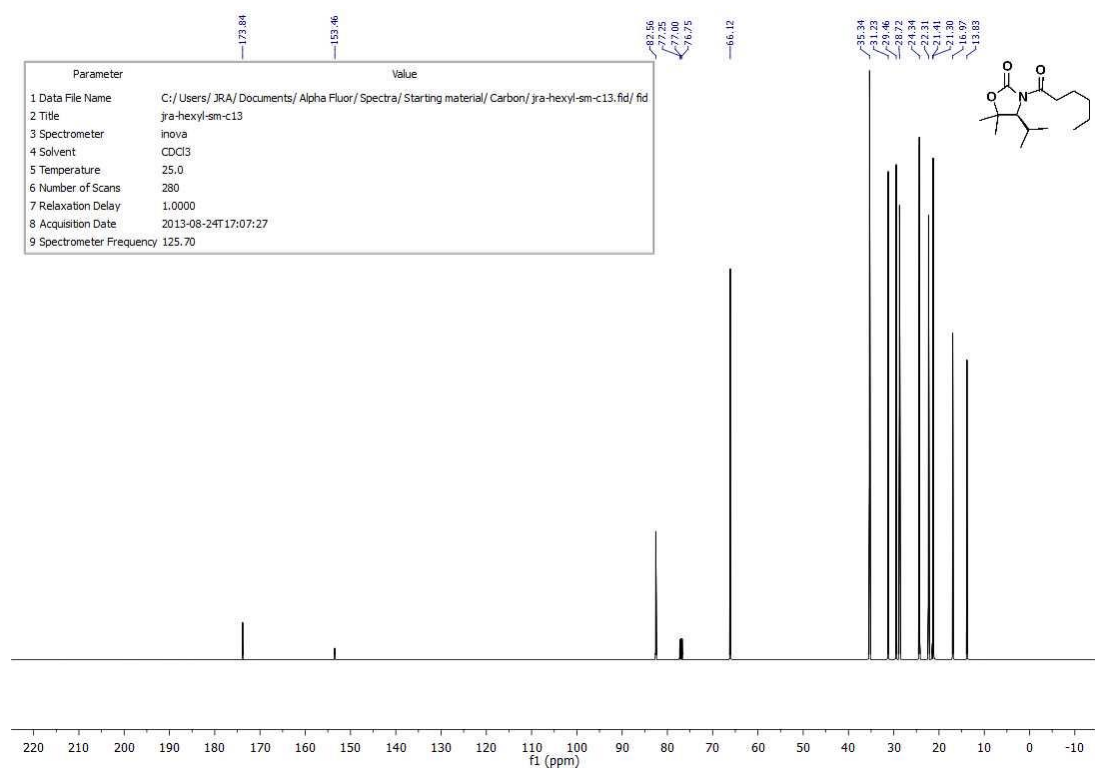
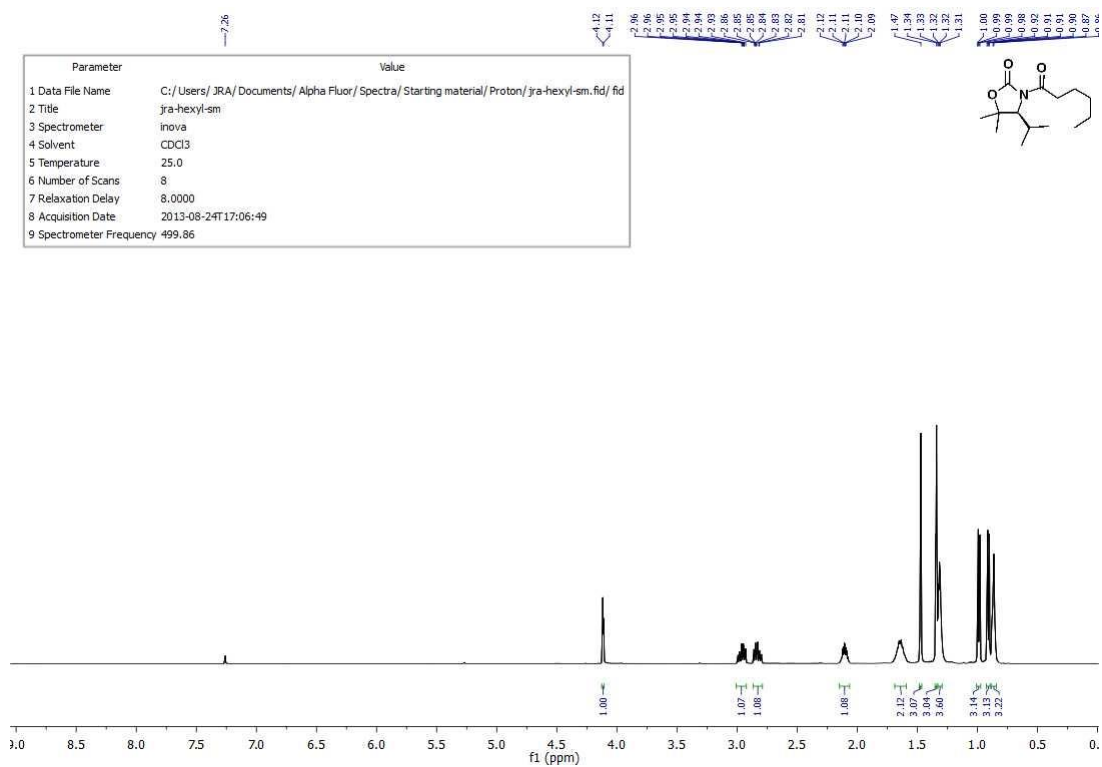
(*S*)-2-Fluoro-2-phenylacetic acid. Lithium hydroxide monohydrate (32.1 mg, 0.765 mmol) was added to a solution of the substrate (0.117 g, 0.373 mmol), hydrogen peroxide (30%, 0.40 mL), and water (0.40 mL) in THF (1.50 mL) at 0 °C, and the mixture was stirred for 5 min. The reaction was warmed to room temperature and stirred for 1 h. The reaction was quenched with aqueous sodium sulfite (1.5 M, 3.0 mL) and HCl (1 M, 3.0 mL) and allowed to stir for 5 min until two transparent layers were visible. The layers were separated

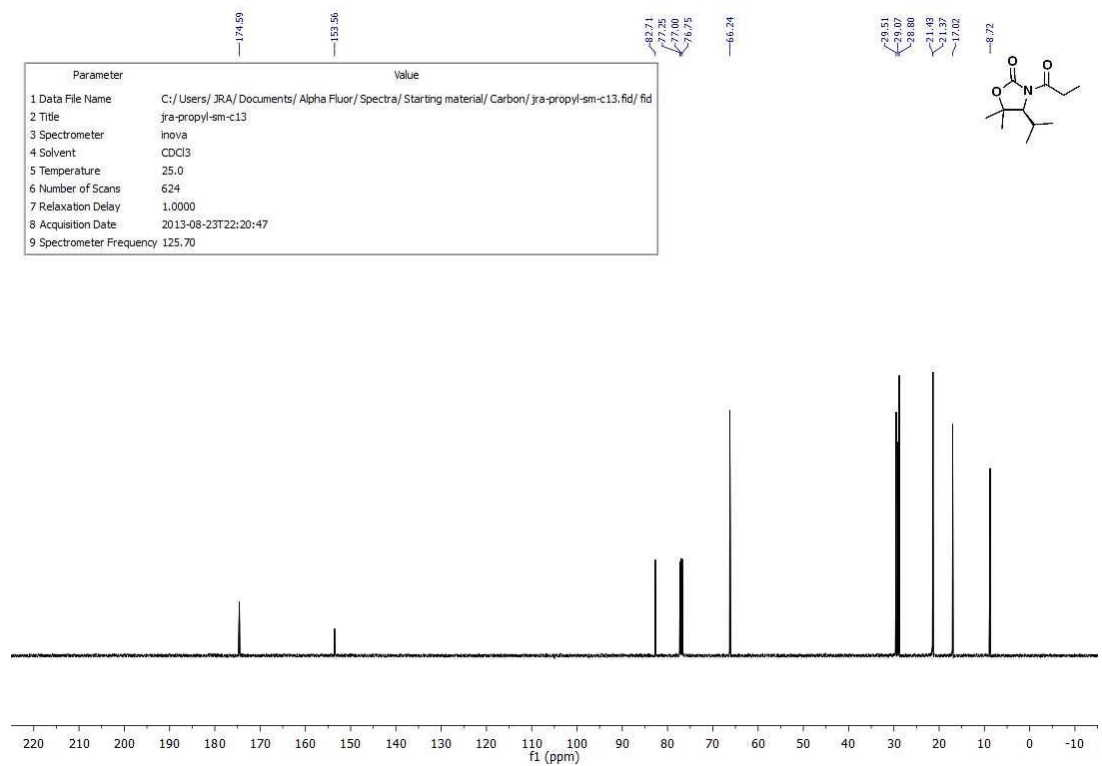
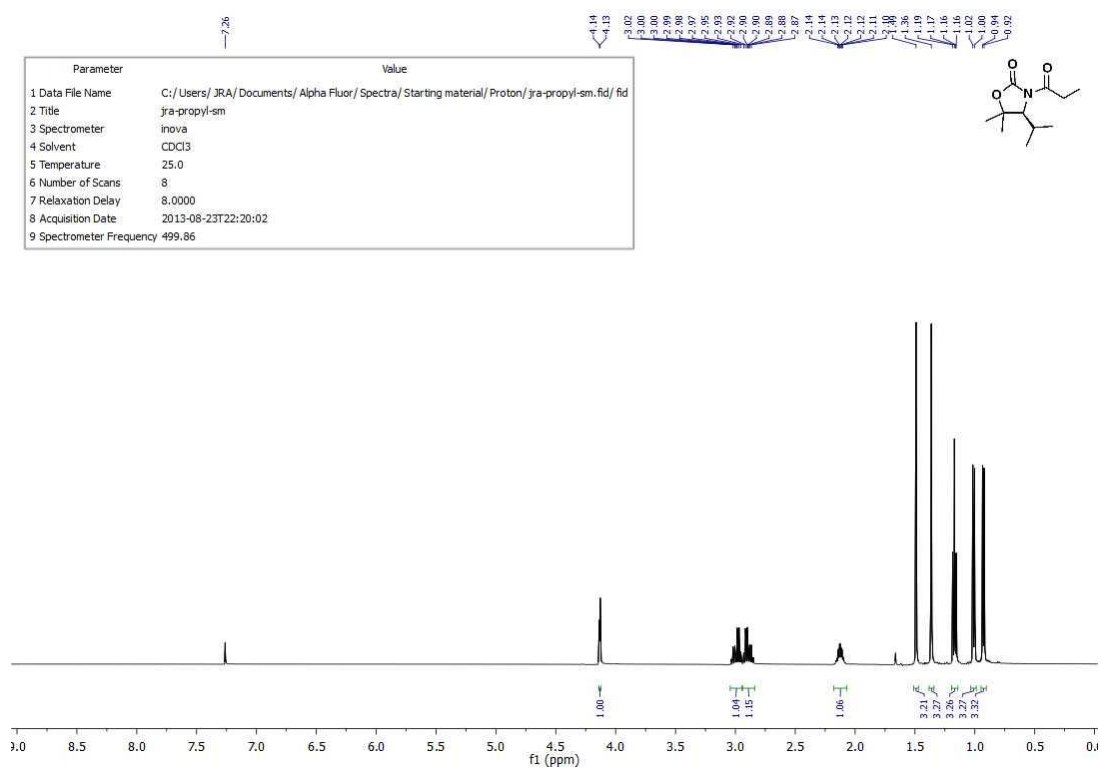
and the aqueous layer was extracted with diethyl ether (3 x 10 mL). The organic layer was extracted with aqueous sodium hydroxide (3 M, 3 x 3 mL) and water (3 x 5 mL). The aqueous extractions were combined and set aside. The organic layer was washed with HCl (1 M), brine, dried with sodium sulfate, and concentrated *in vacuo* to recover the oxazolidinone auxiliary (56.6 mg, 0.36 mmol, 97%). The previously saved aqueous layers were acidified with aqueous HCl (1 M). The aqueous layer was extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine, dried with sodium sulfate, and concentrated *in vacuo* to afford the desired pure carboxylic acid (55.2 mg, 0.358 mmol, 96%). $\alpha_D^{21} + 116.06$ (c 0.843, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ (ppm): 9.23 (s, 1H), 7.46 (d, *J* = 34.7 Hz, 5H), 5.83 (d, *J* = 47.4 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ (ppm): 174.06 (d, *J* = 28.0 Hz), 133.42 (d, *J* = 20.5 Hz), 129.90 (d, *J* = 30.1 Hz), 128.87 (d, *J* = 31.6 Hz), 126.65 (d, *J* = 33.8 Hz), 88.78 (dd, *J* = 186.7, 15.5 Hz). ¹⁹F NMR (564 MHz, CDCl₃) δ (ppm): -180.78 (d, *J* = 47.8 Hz). HRMS-EI (*m/z*): [M]⁺ calcd for C₈H₇FO₂, 154.0430; found, 154.0434.

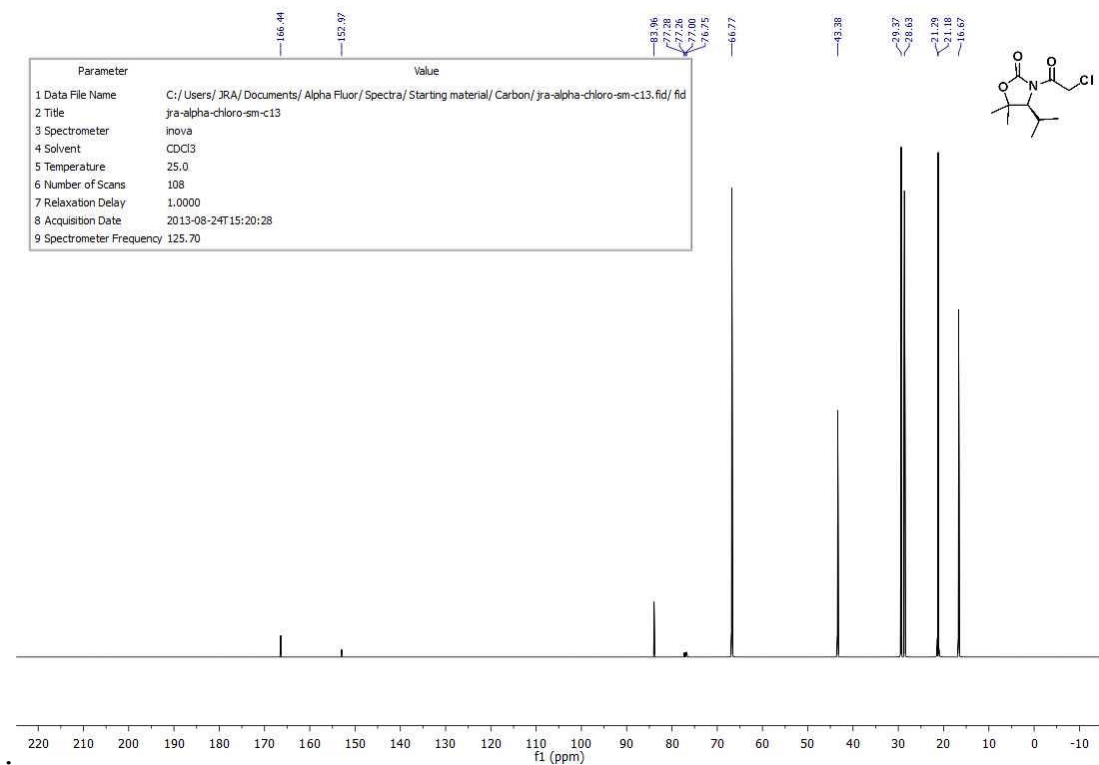
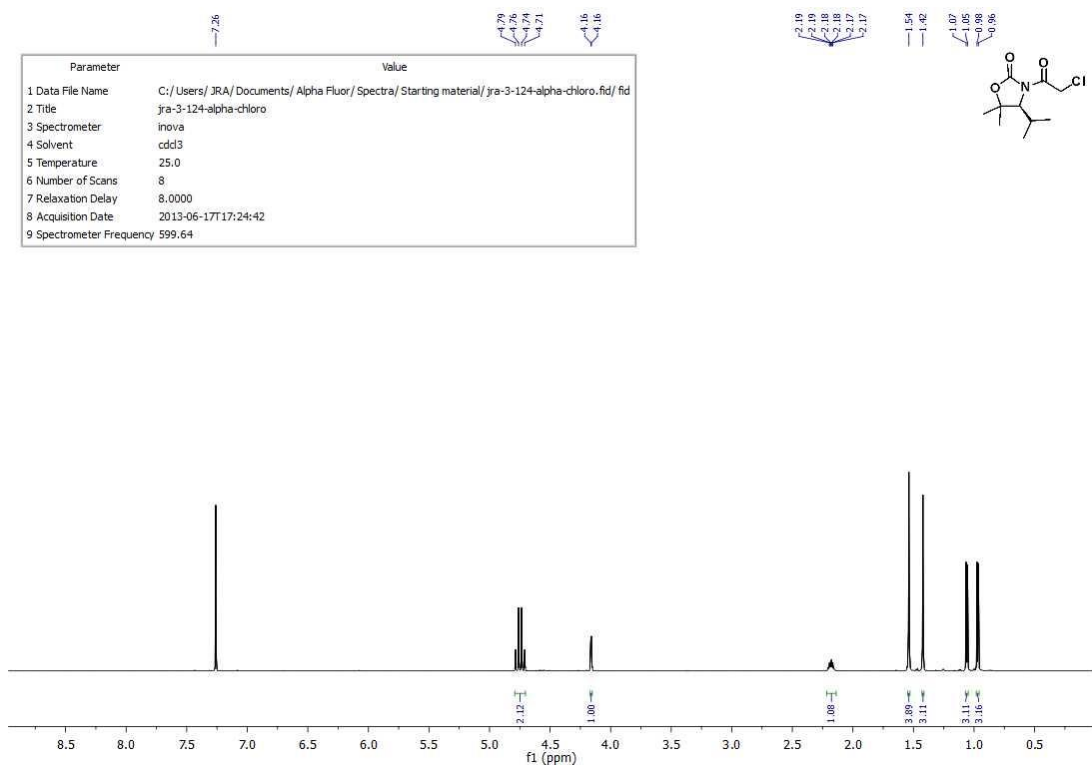
Determination of *er* for the acid: A solution of the (*S*)-2-fluoro-2-phenylacetic acid (1.0 equiv) in diethyl ether (0.2 M) was added to a solution of lithium aluminum hydride (4.0 equiv) in diethyl ether (0.5 M) at 0 °C and the mixture was stirred for 10 min. The reaction mixture was warmed to room temperature and stirred for 10 min and quenched using the Feiser workup: the reaction was cooled to 0 °C; H₂O (1:1 volume/weight to LiAlH₄) was added dropwise to the reaction (CAUTION: highly exothermic) and stirred for 5 min. A solution (1:1 by volume/weight to LiAlH₄) of aqueous NaOH (15 wt% NaOH in H₂O) was added dropwise and stirred for 5 min. Finally H₂O (3:1 by volume/weight to LiAlH₄) was

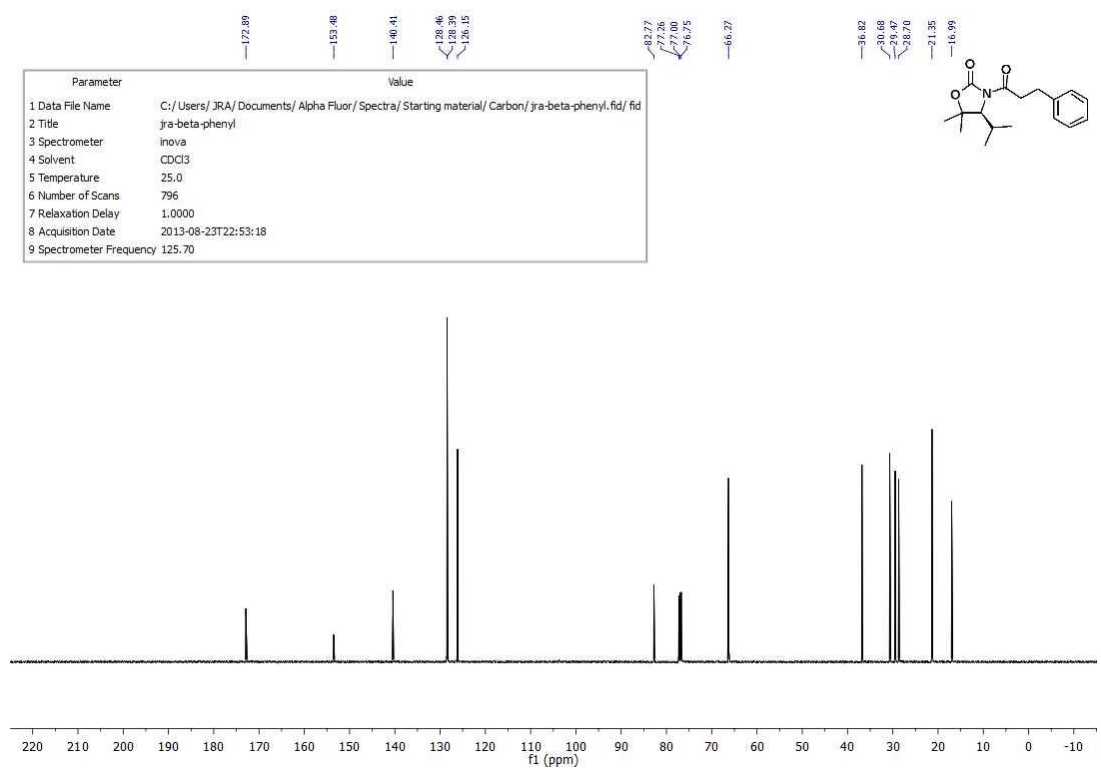
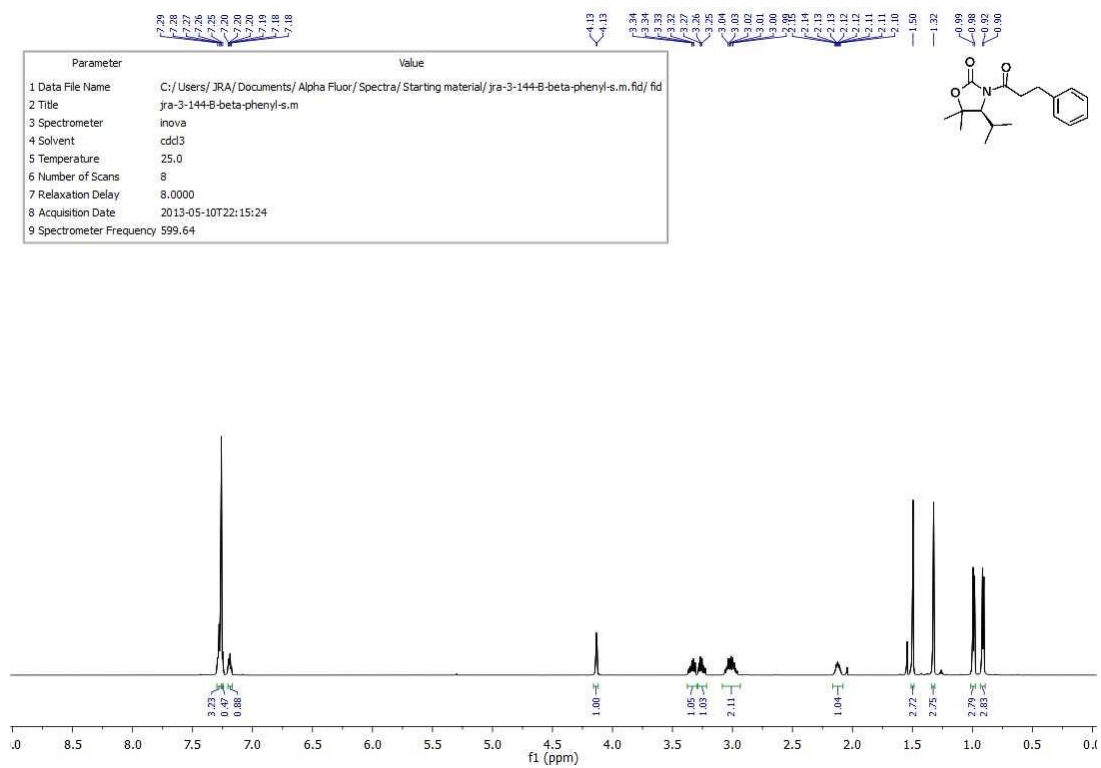
added dropwise. The solution was warmed to room temperature and allowed to stir for 1 h, until a white precipitate forms. The reaction mixture was filtered and concentrated *in vacuo*. No further purification was done.

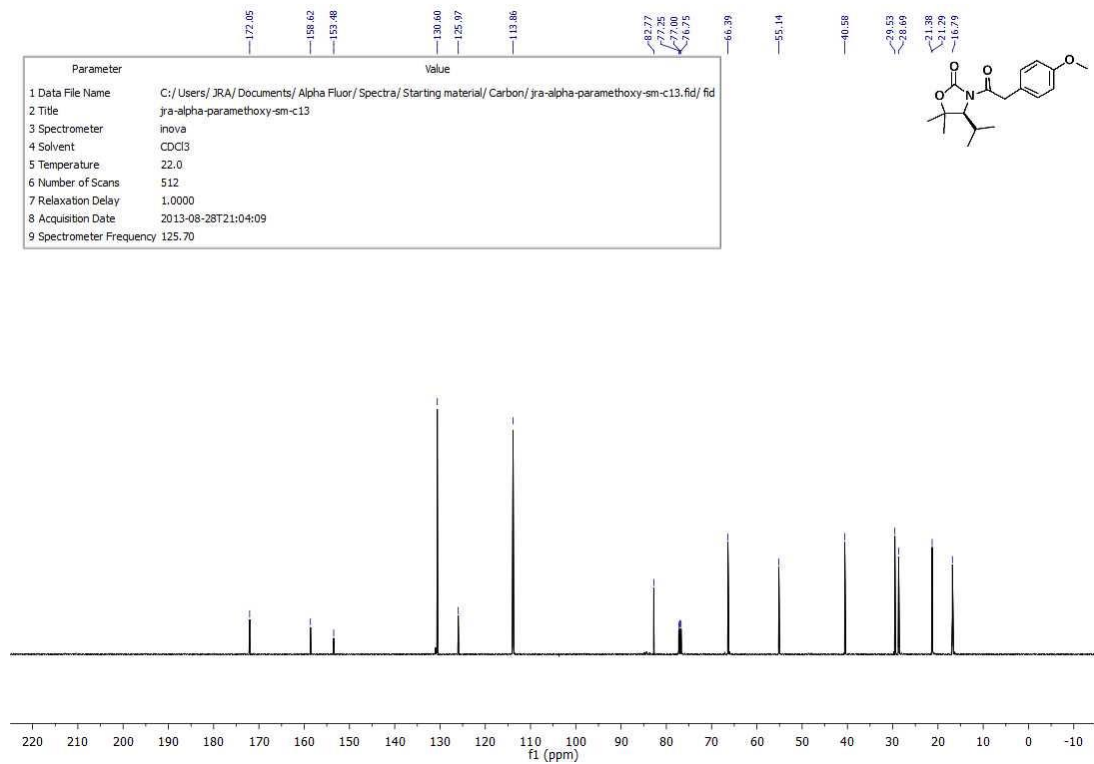
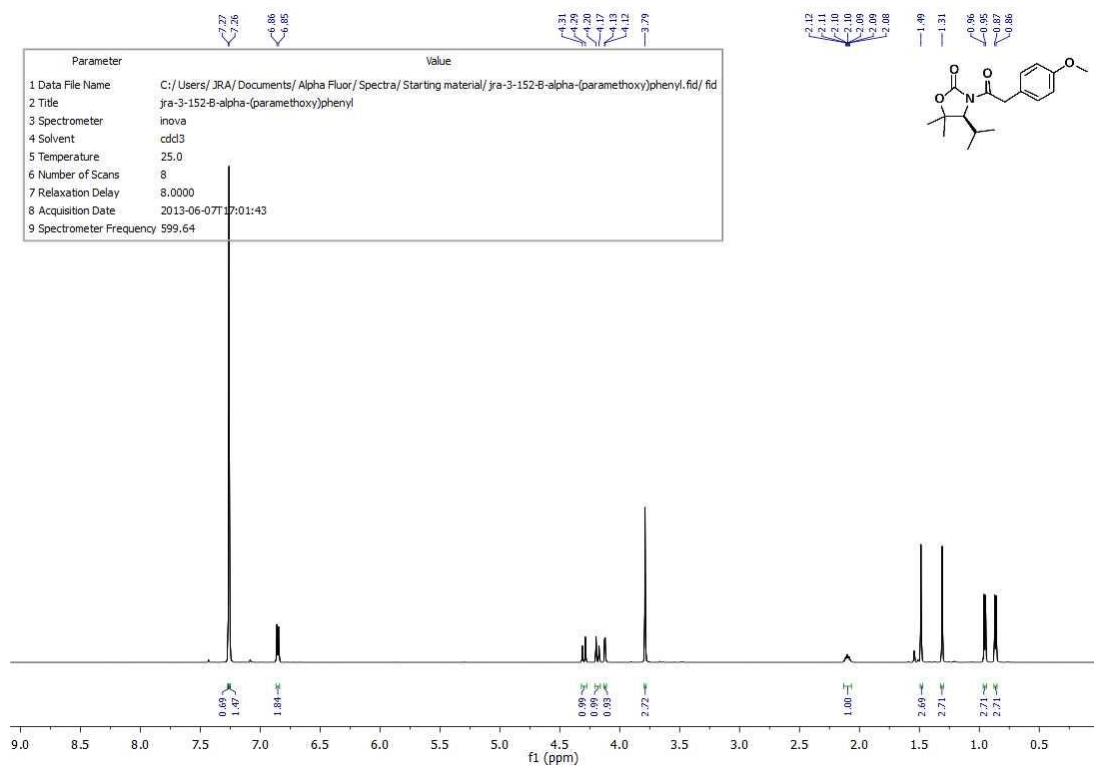
2-Naphthoyl chloride (5.0 equiv.) was added to a solution of the crude alcohol, triethylamine (5.0 equiv.), and 4-dimethylaminopyridine (1.0 equiv.) in dichloromethane (0.1 M) at 0 °C. After 10 min, the reaction was warmed to room temperature and stirred for 30 min. The mixture was quenched with aqueous ammonium chloride and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine, dried with sodium sulfate, concentrated *in vacuo*, and purified by column chromatography (silica, 12.5% ethyl acetate in hexanes) to afford the desired naphthoyl ester derivative. HPLC analysis of the 2-naphthoyl ester derivative (OJ-H, 2.5% *i*PrOH - hexanes, 1.0 mL/min, 254 nm) indicated a 1.1:98.9 ratio: R_T (minor) = 35.9 minutes, R_T (major) = 46.4 minutes.

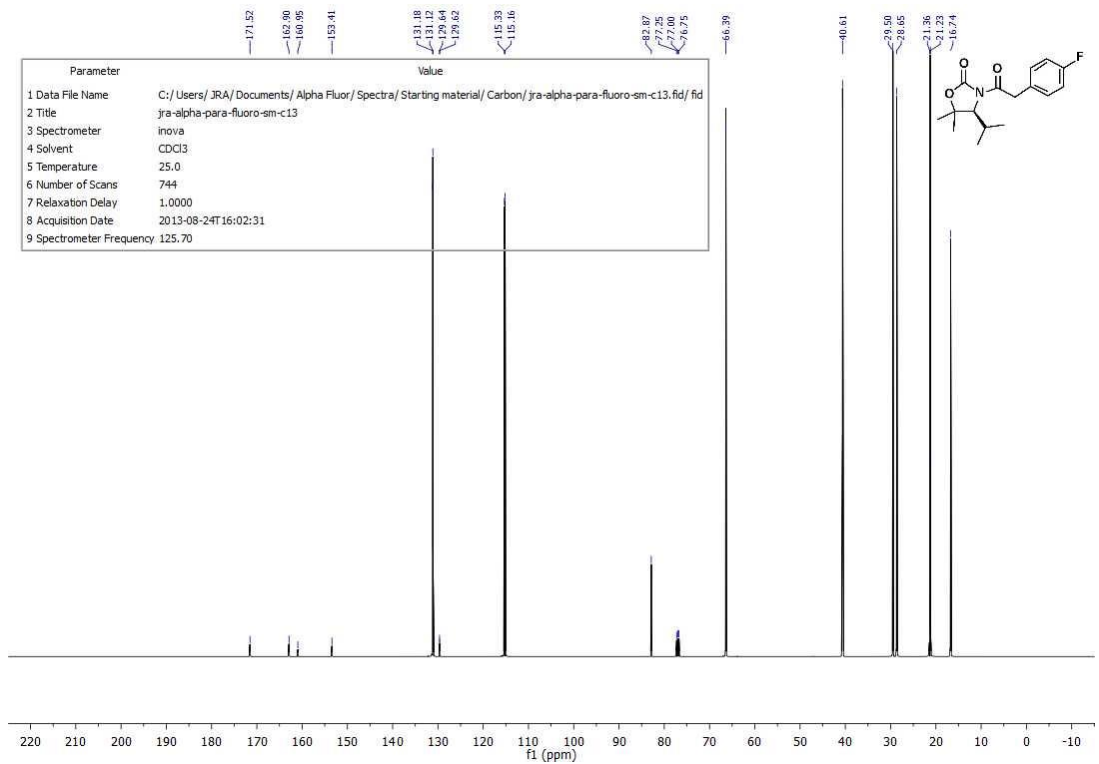
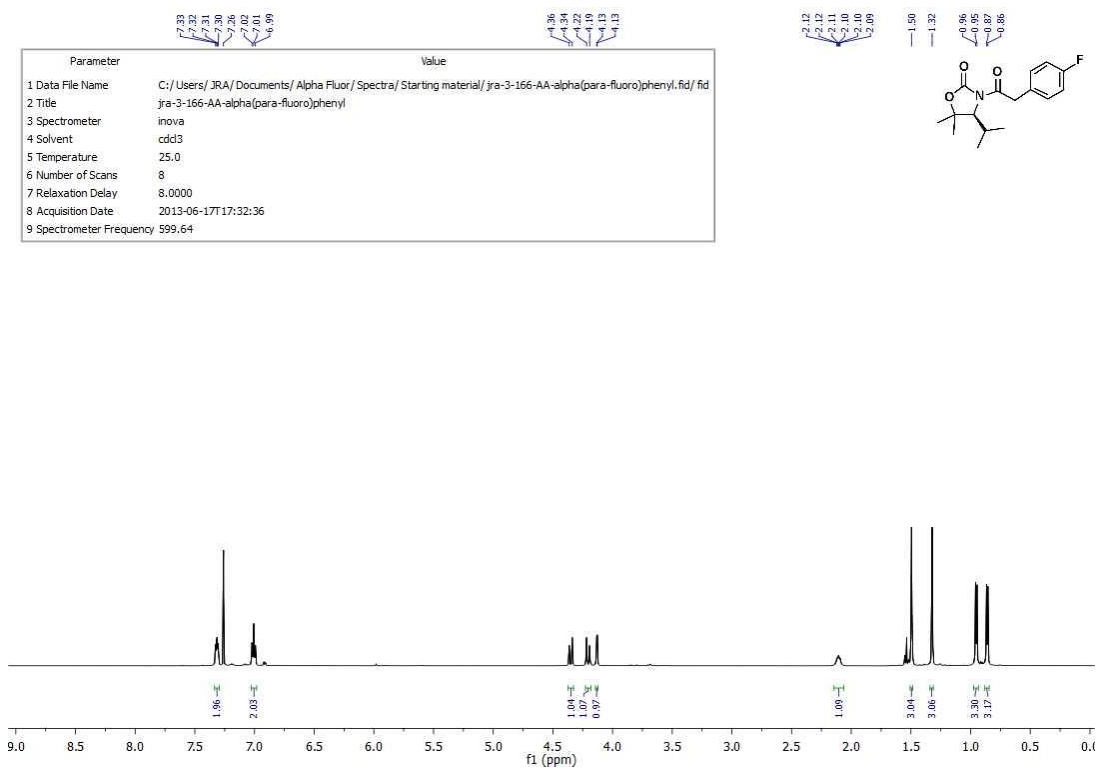


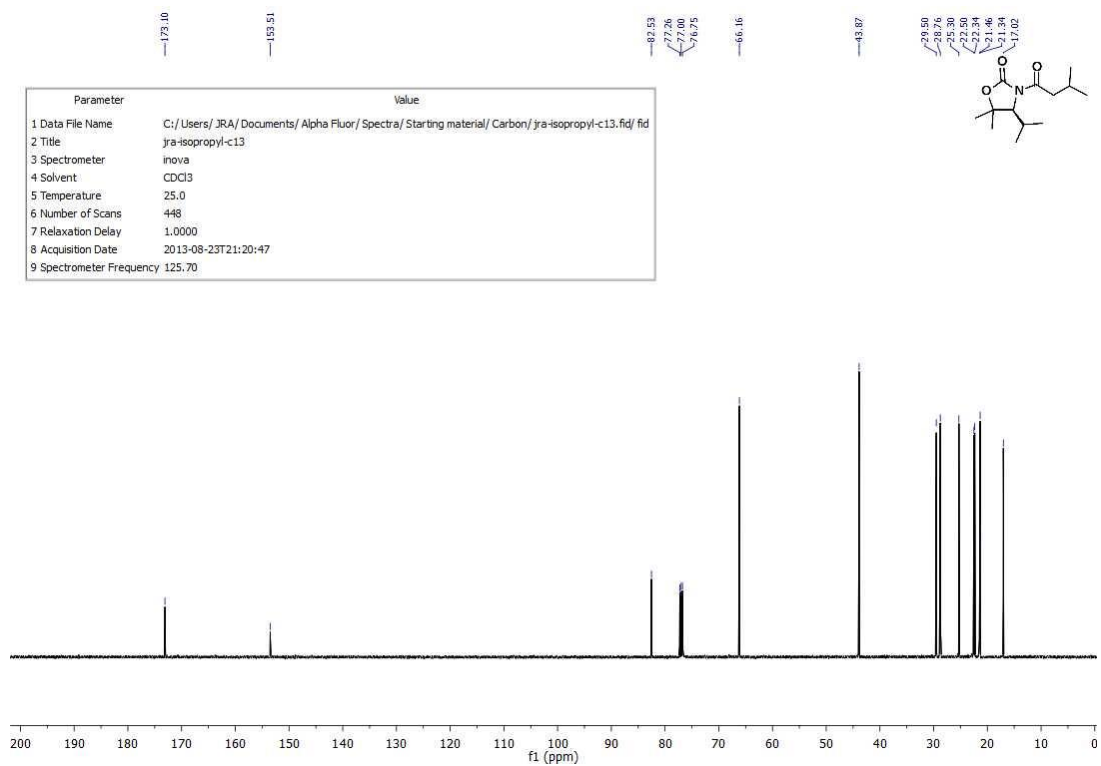
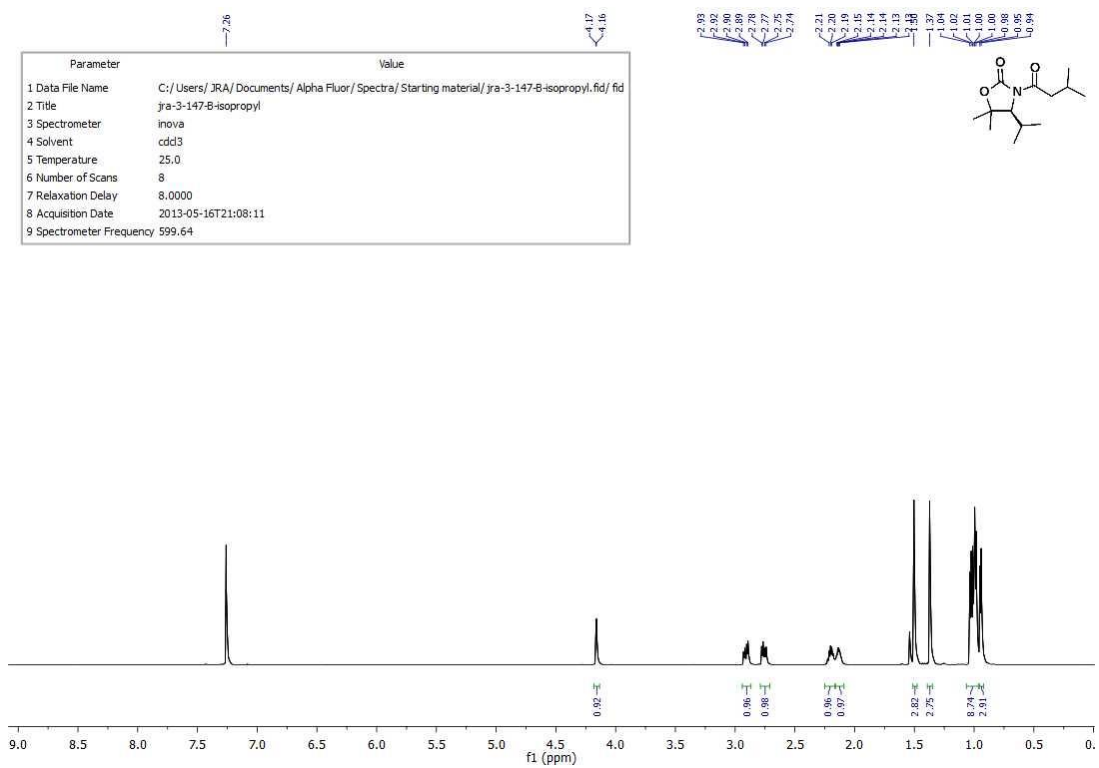


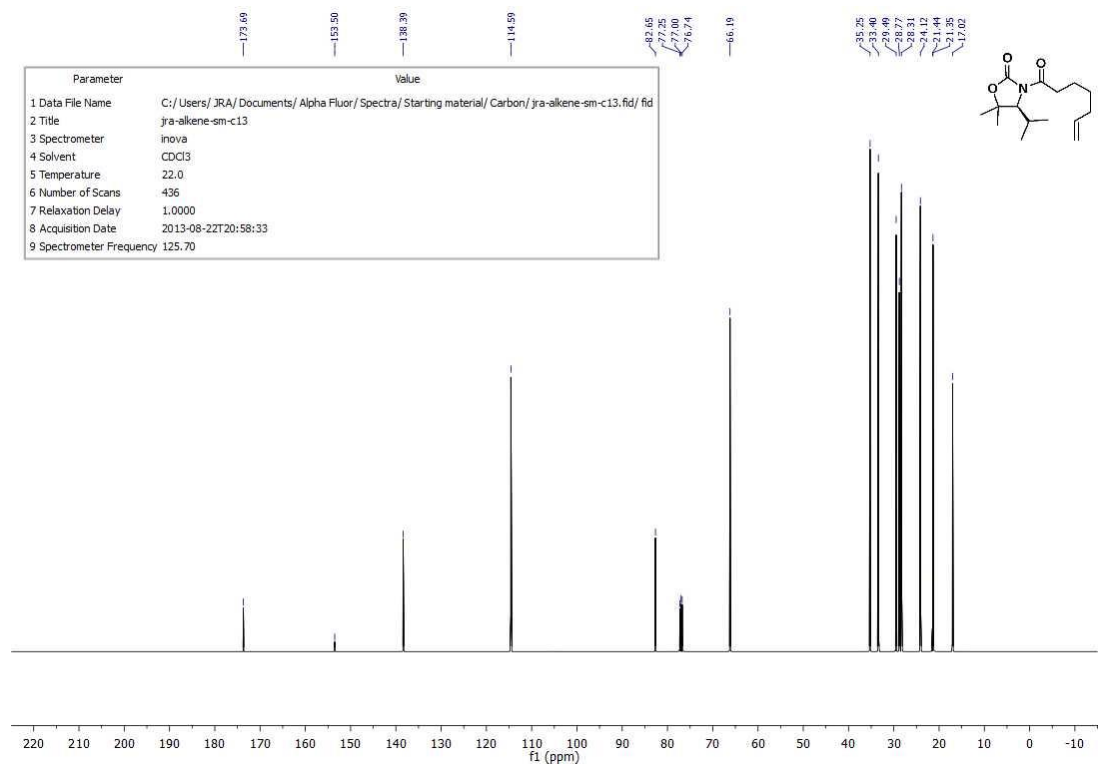
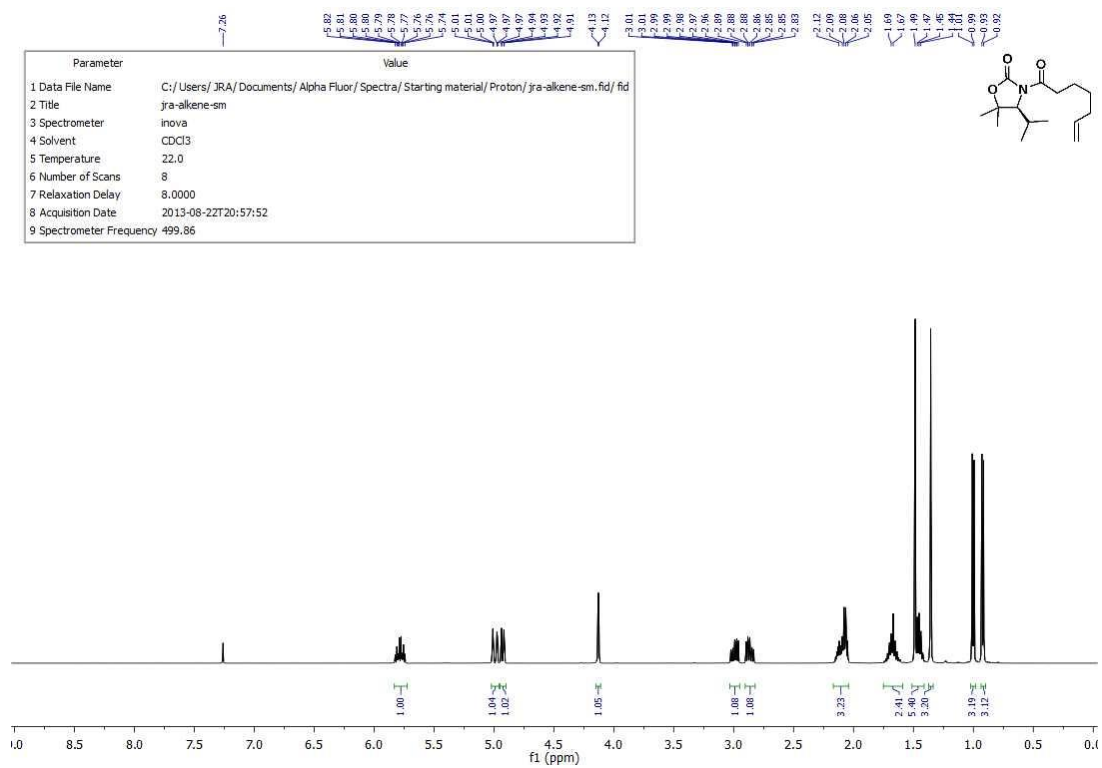


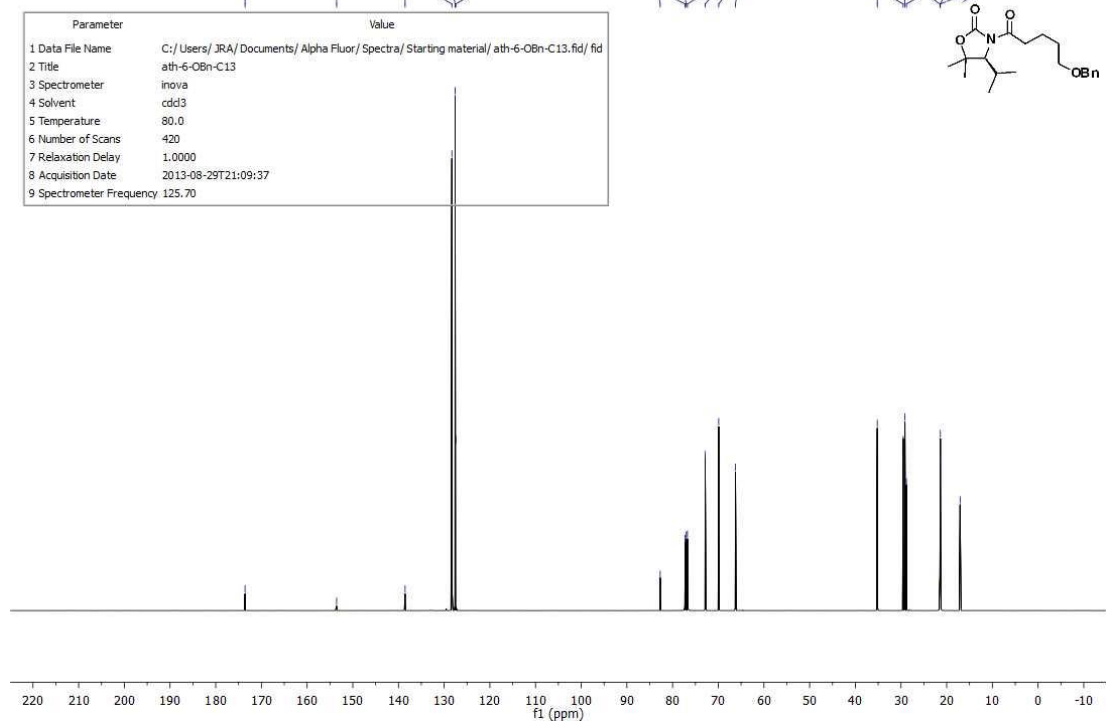
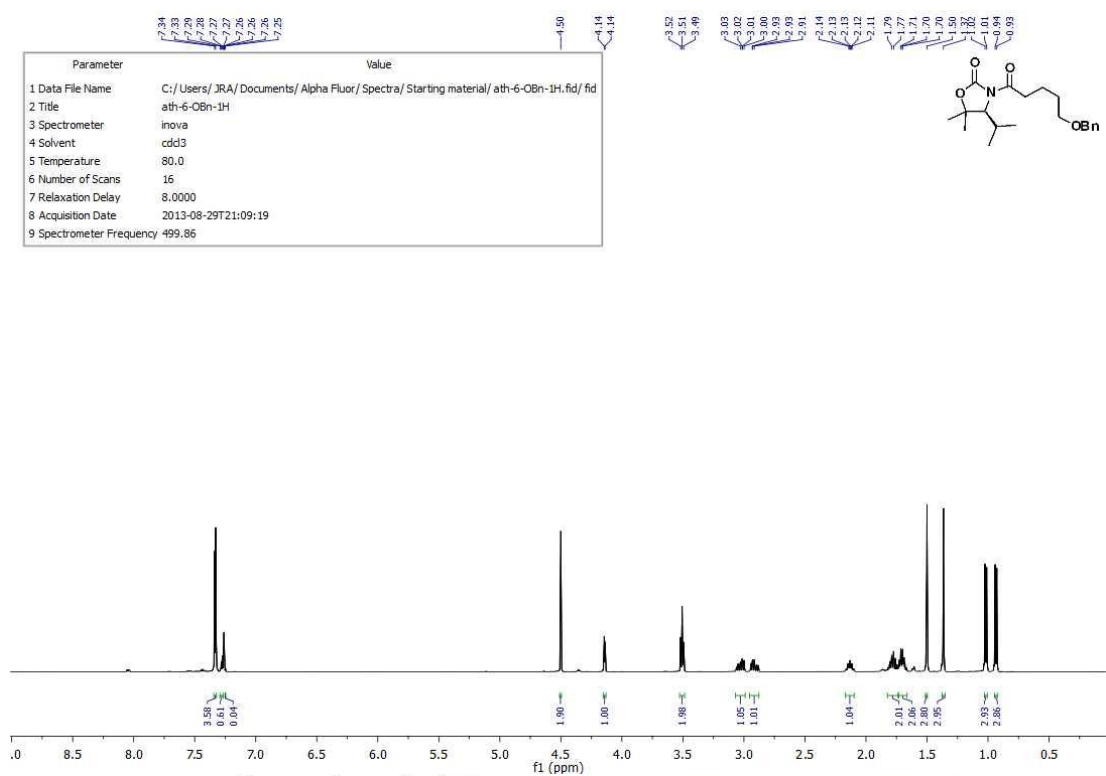


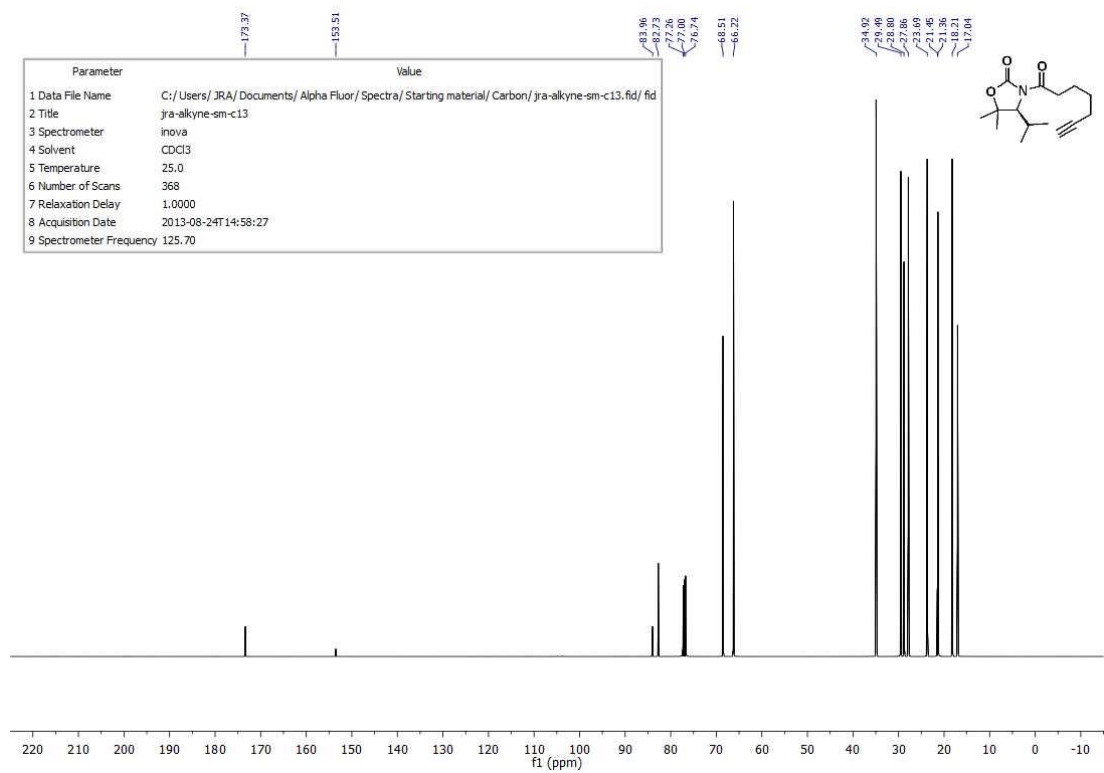
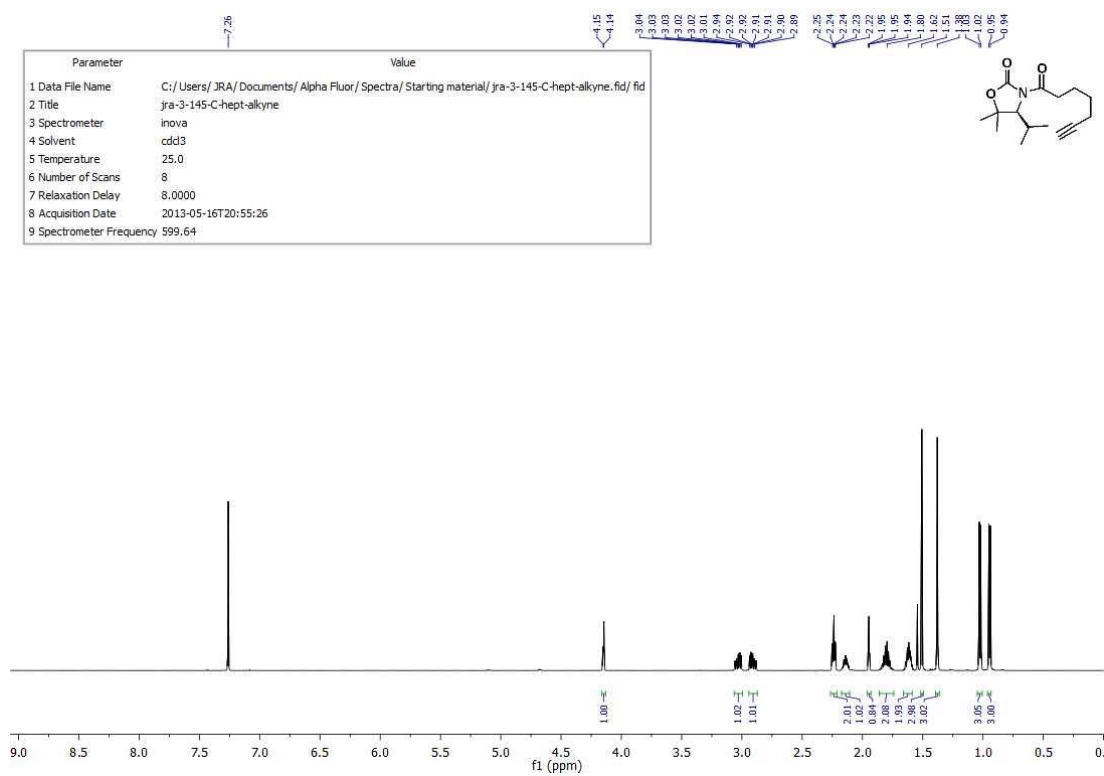


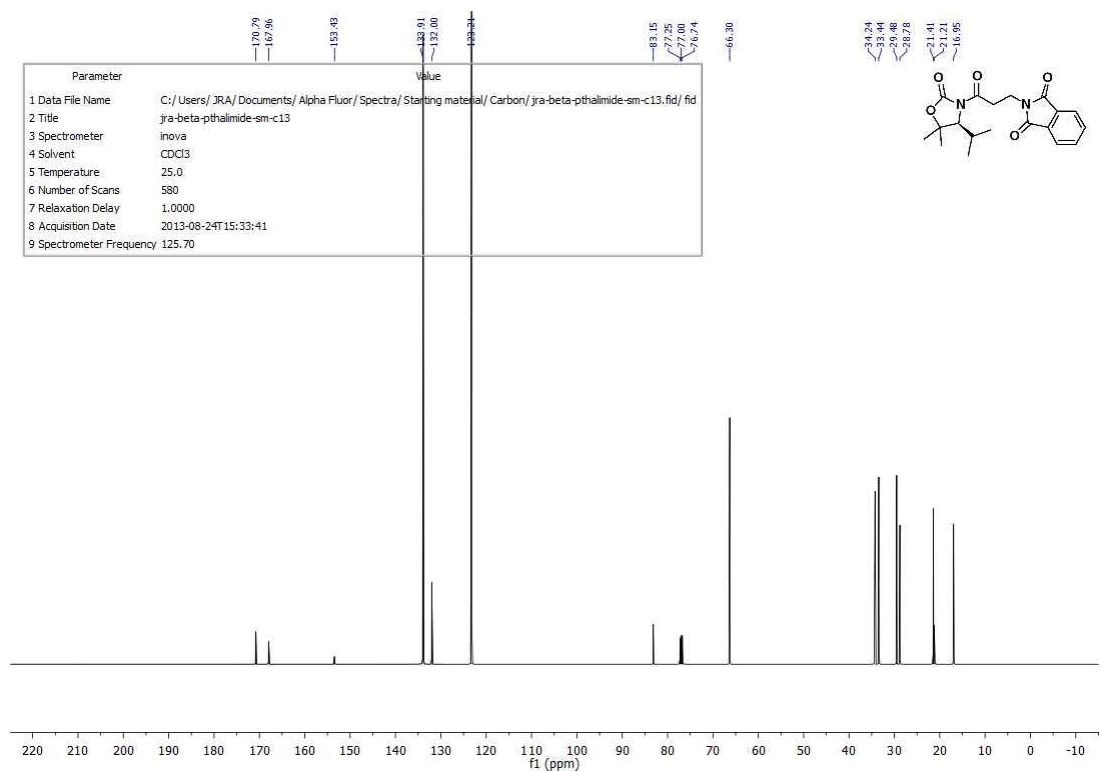
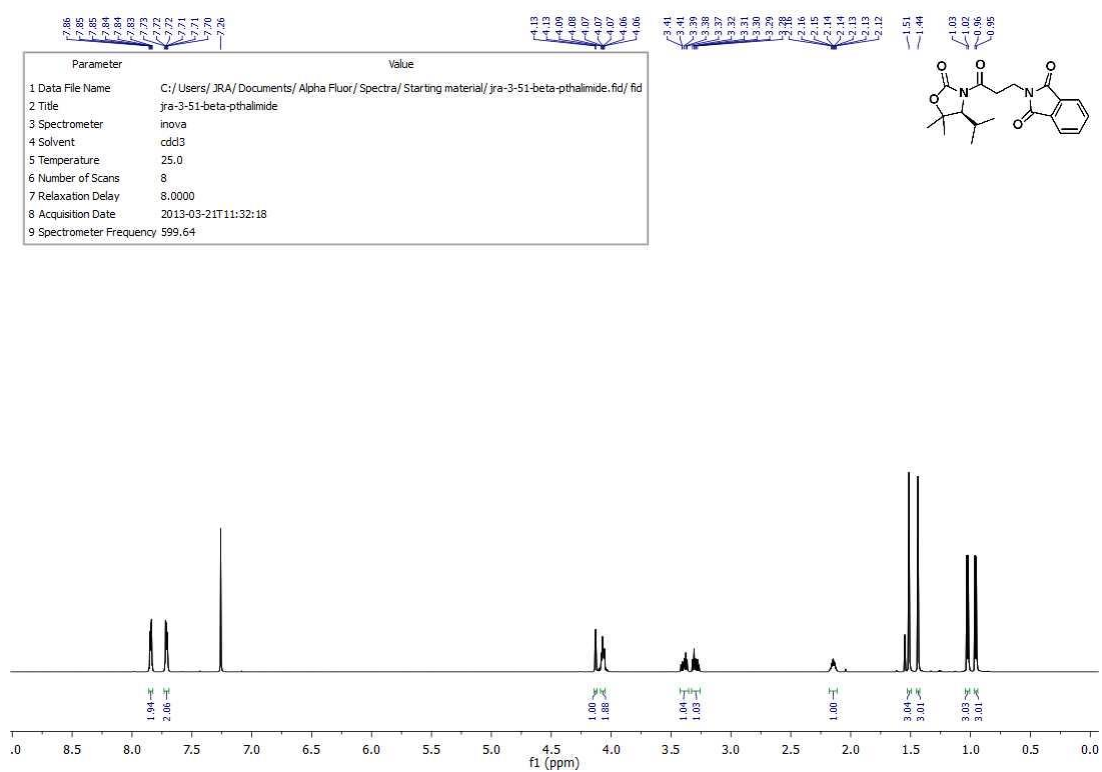


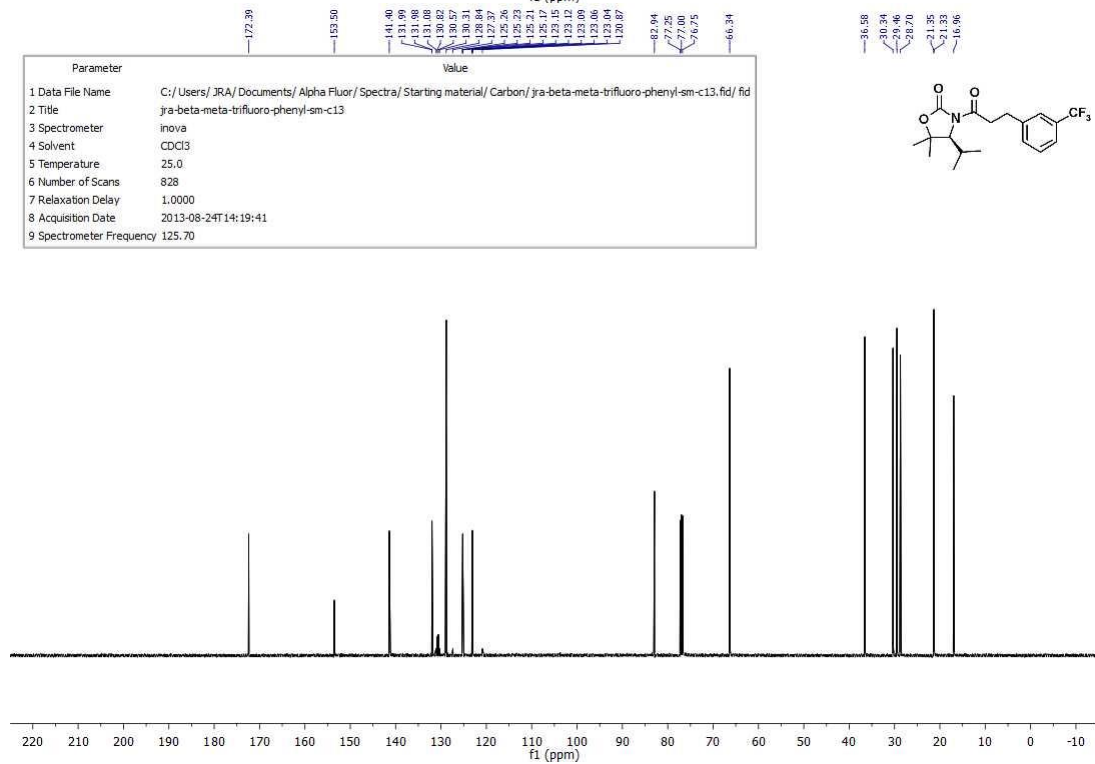
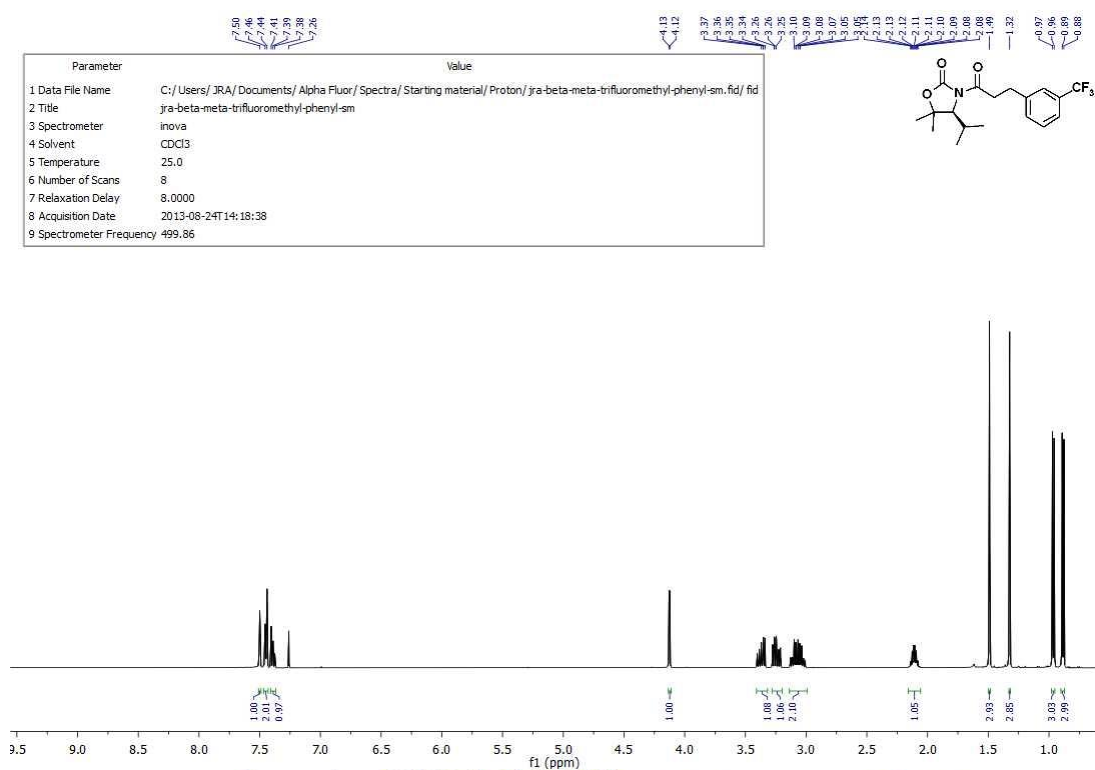


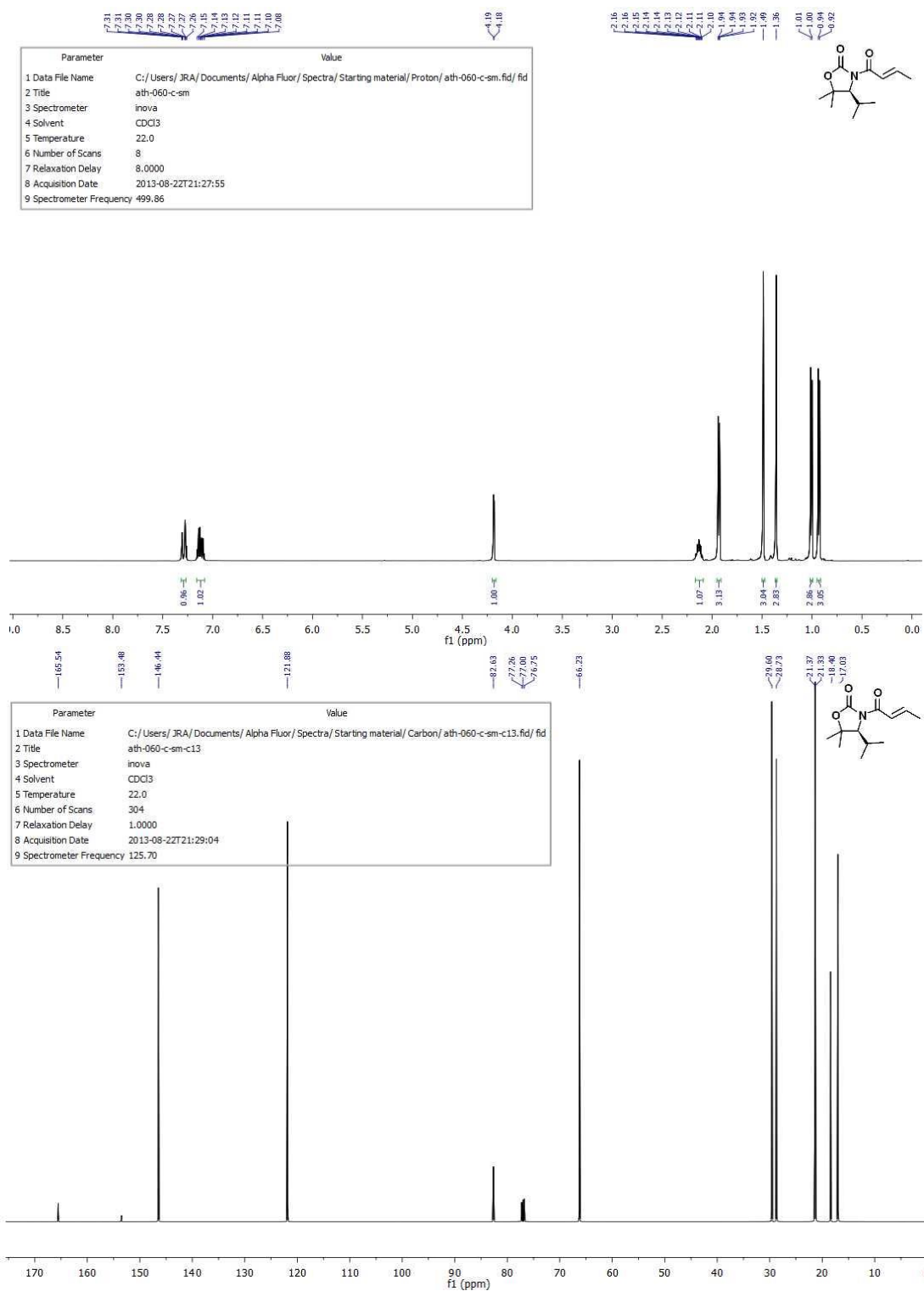


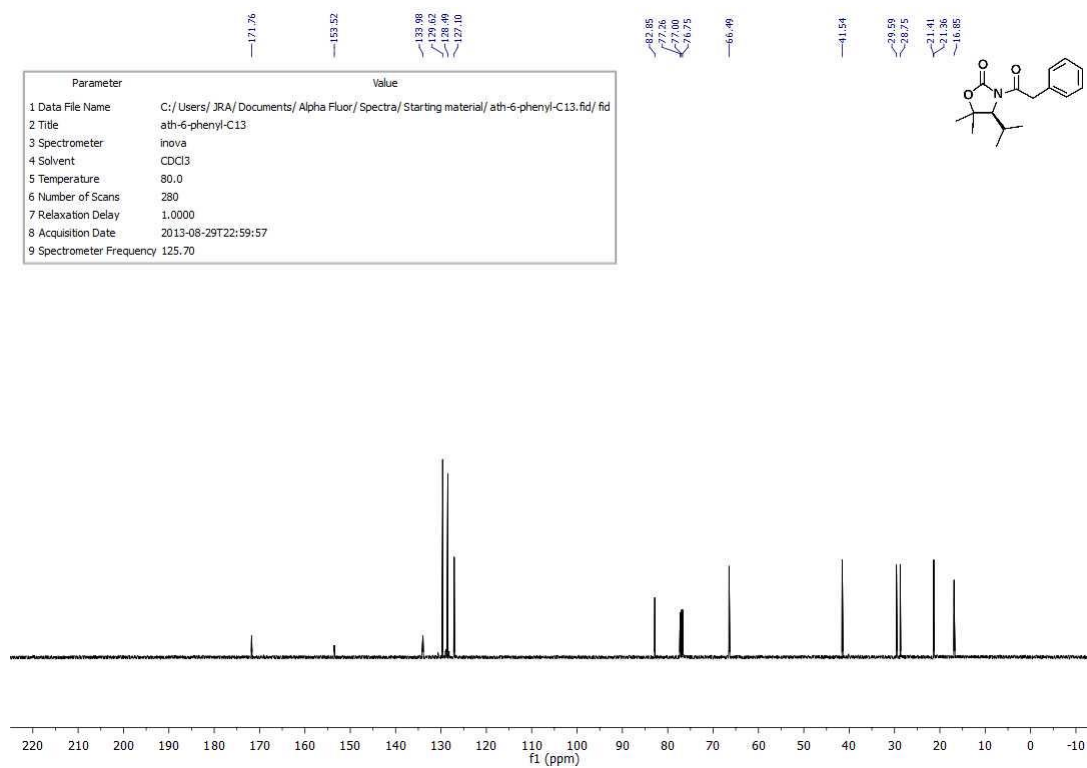
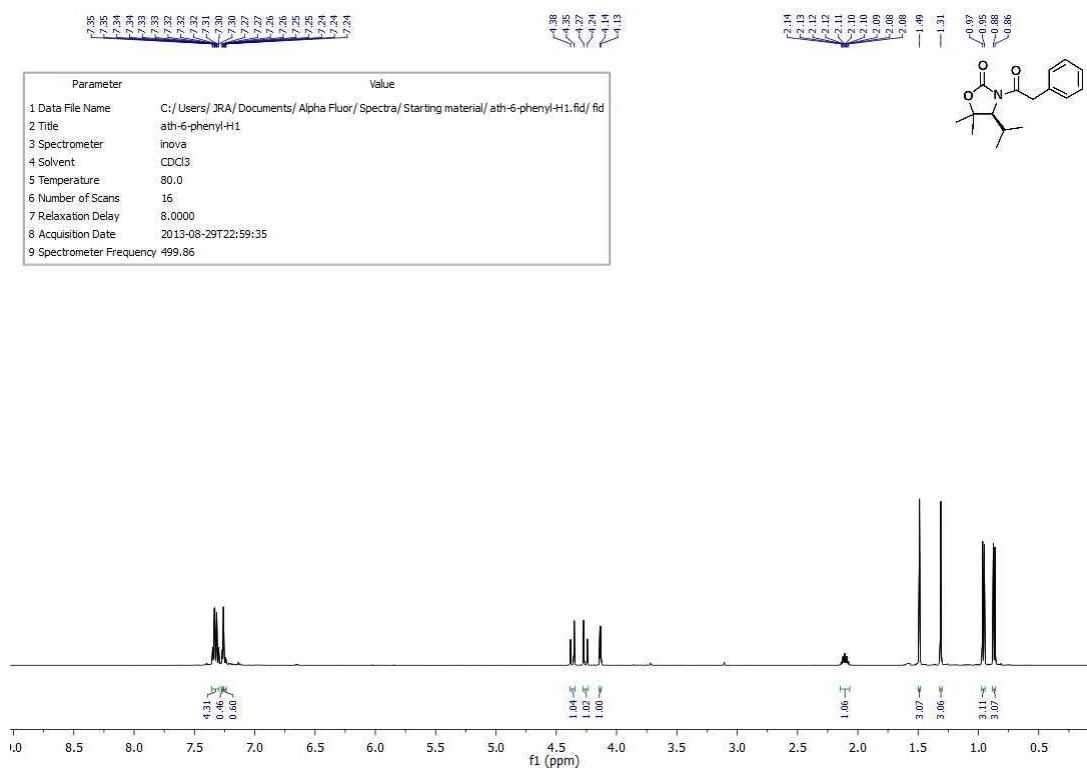


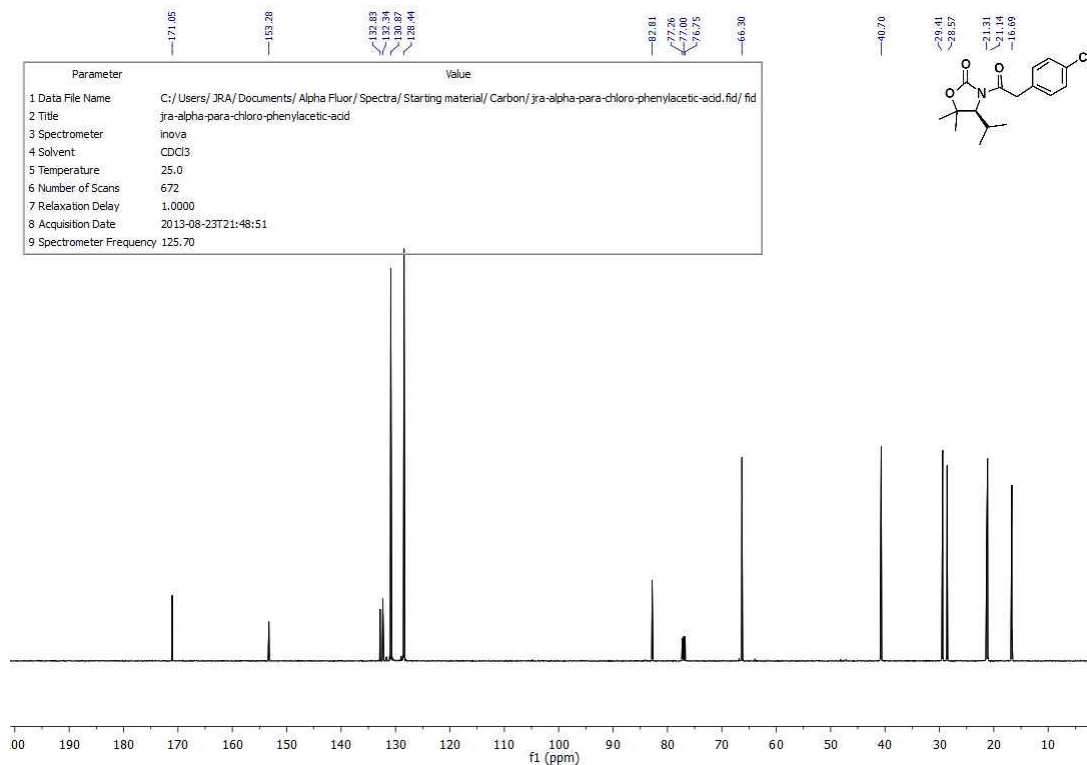
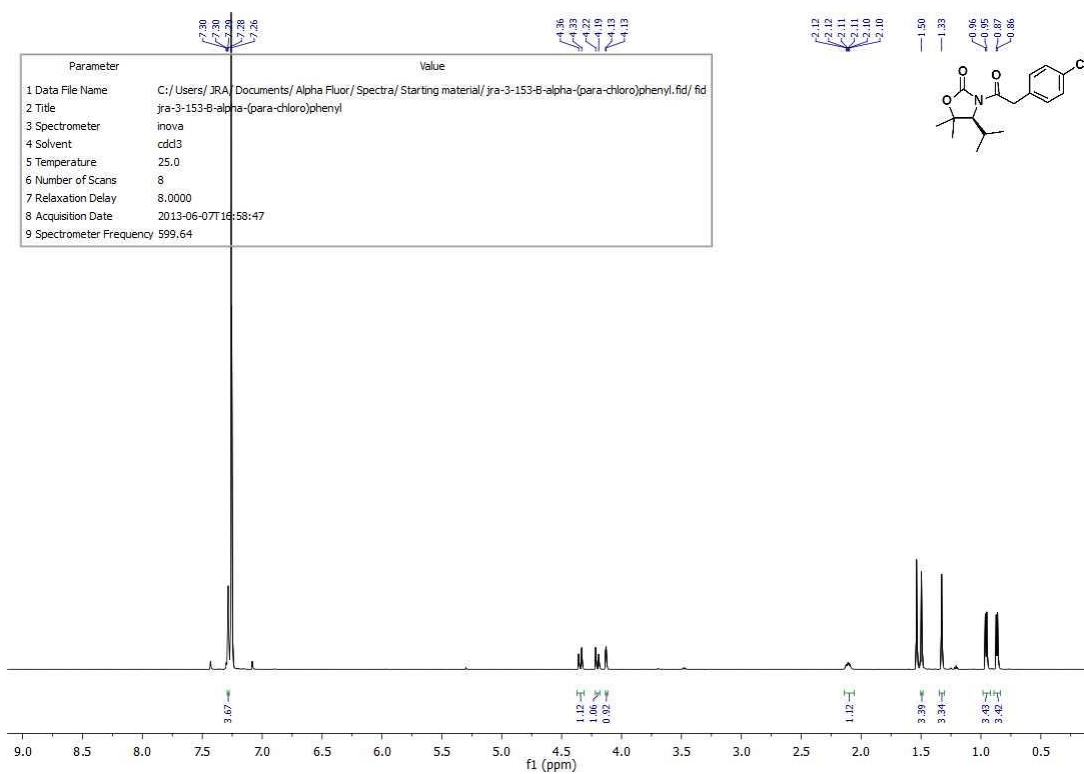




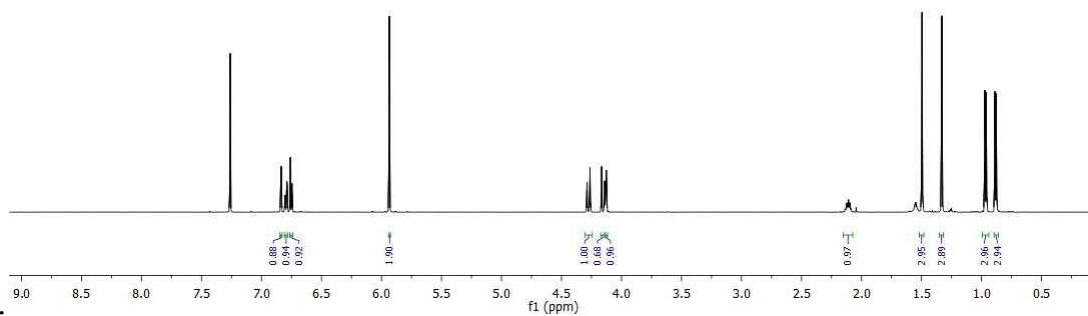
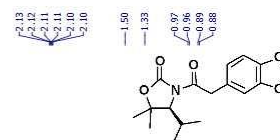




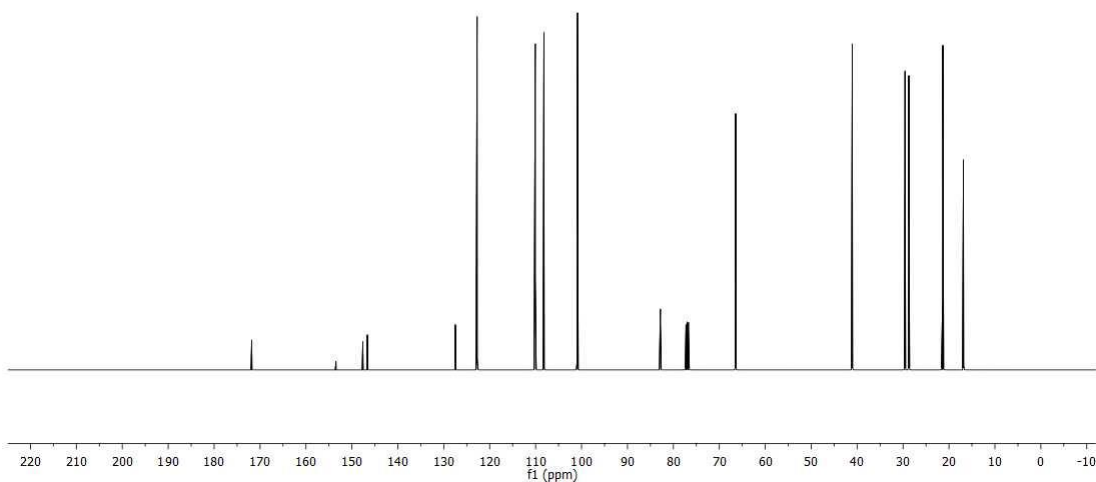
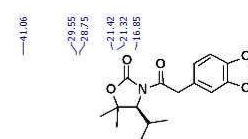


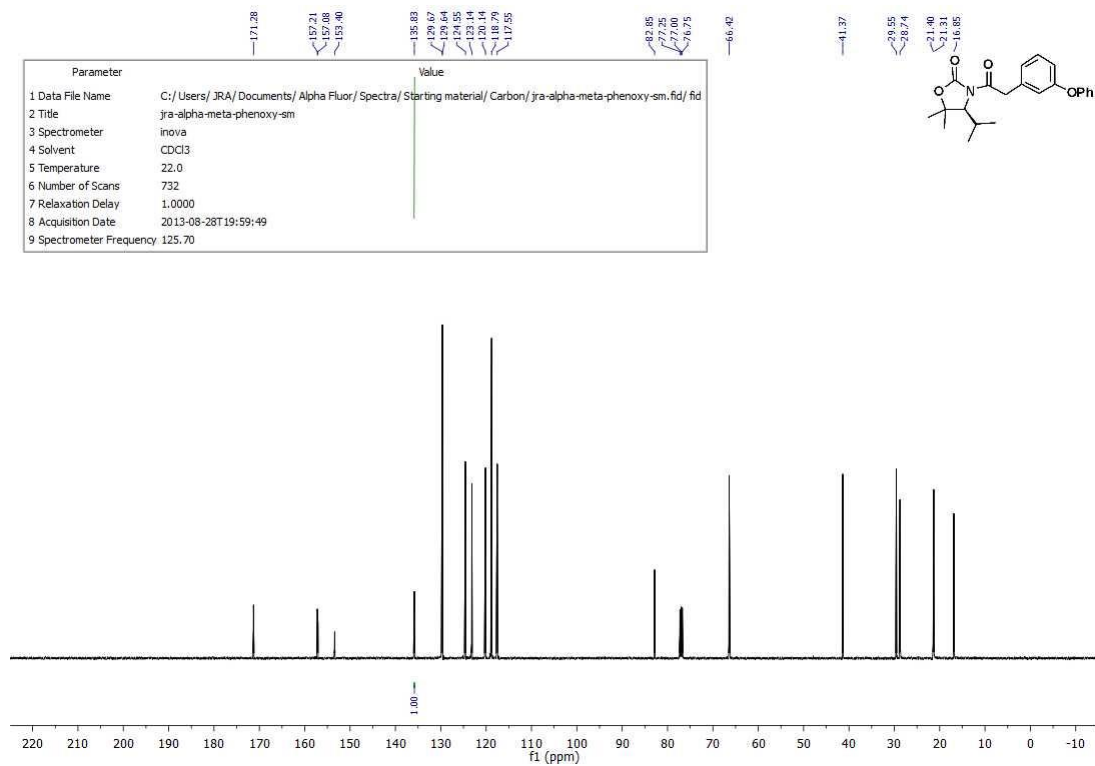
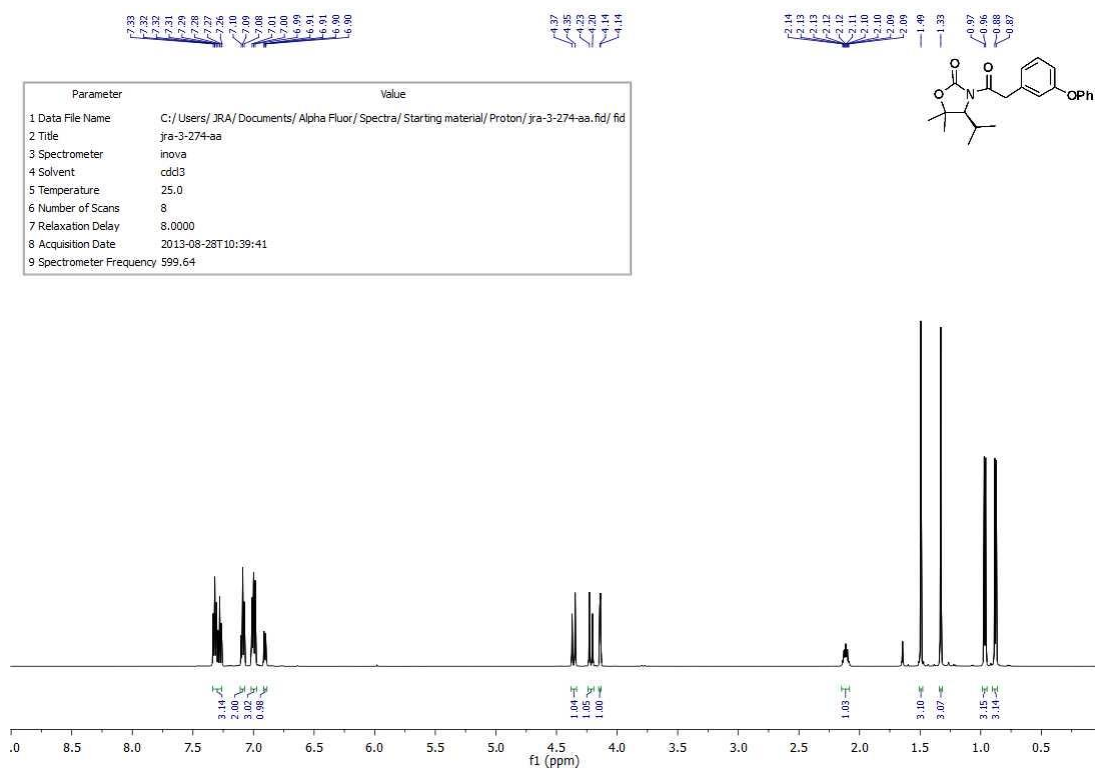


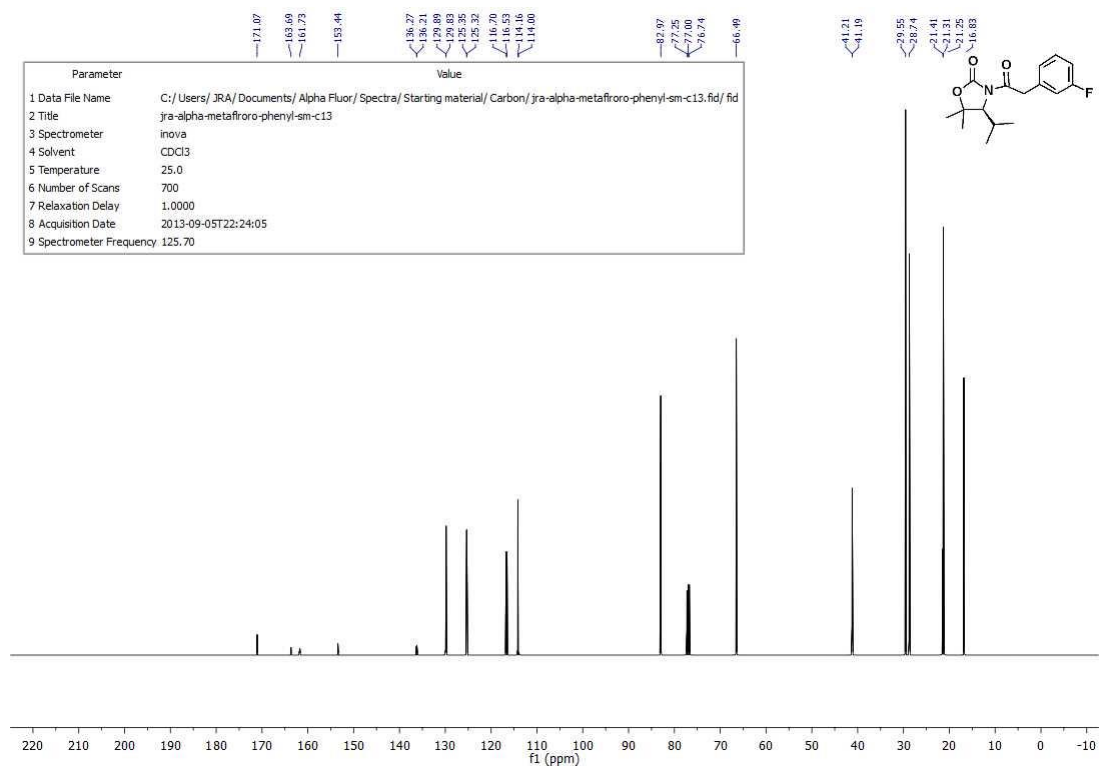
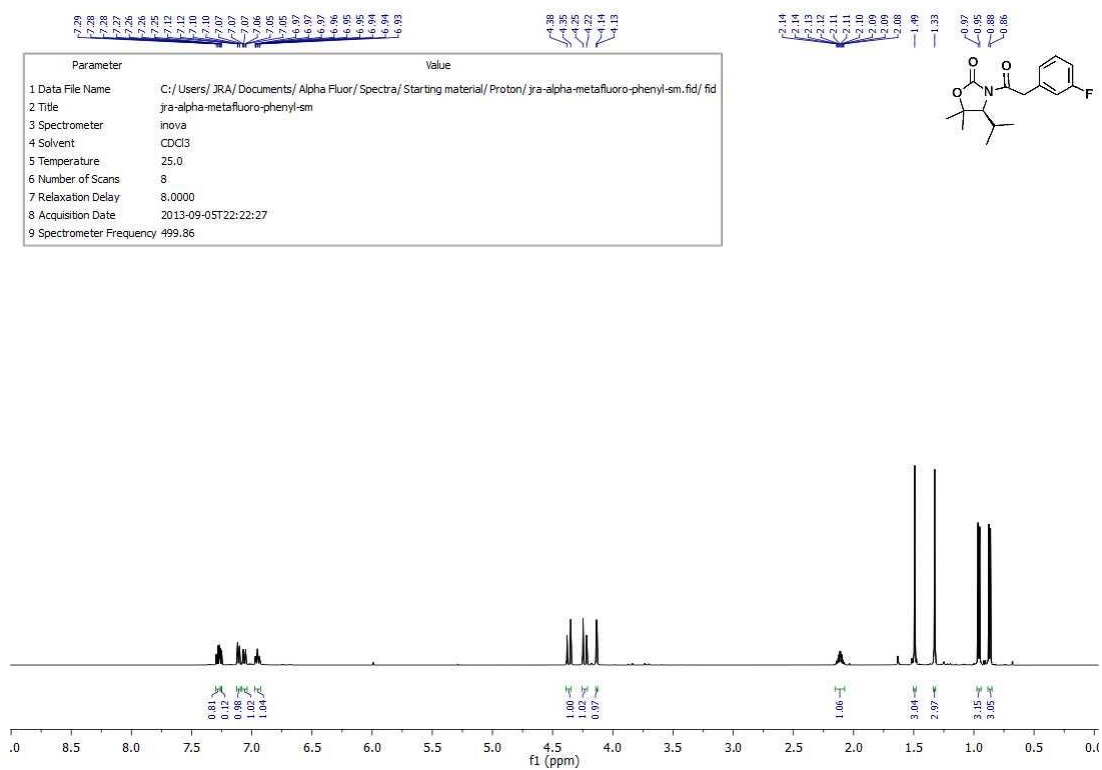
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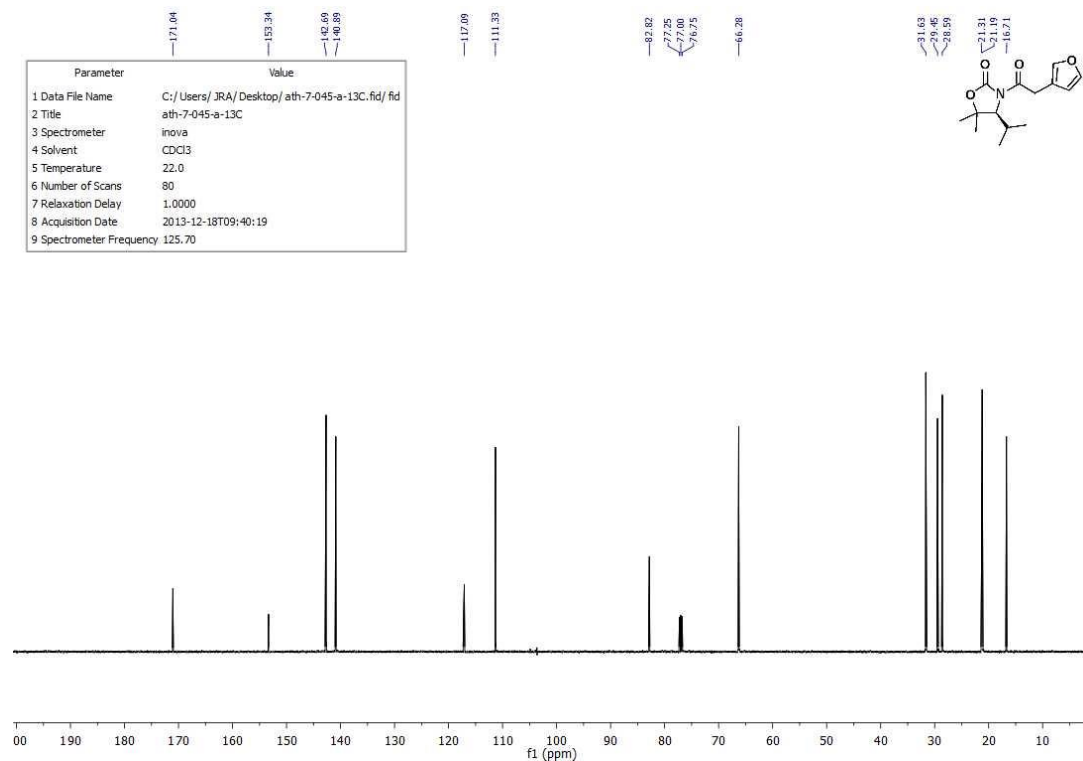
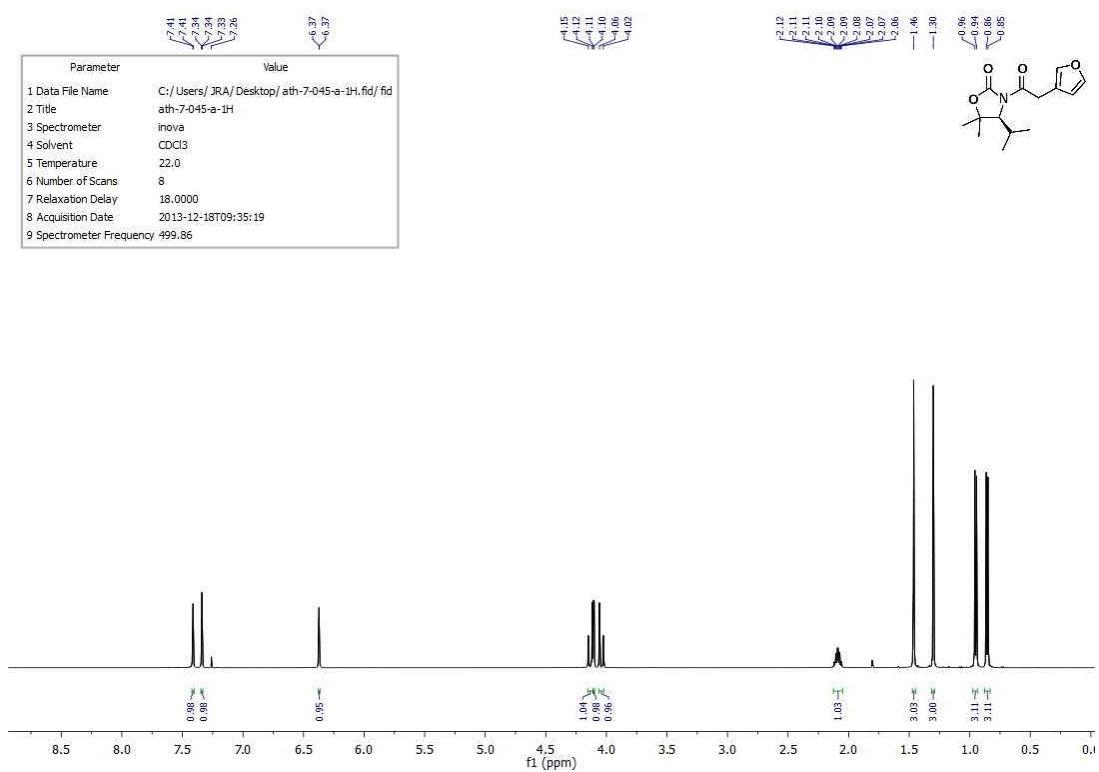


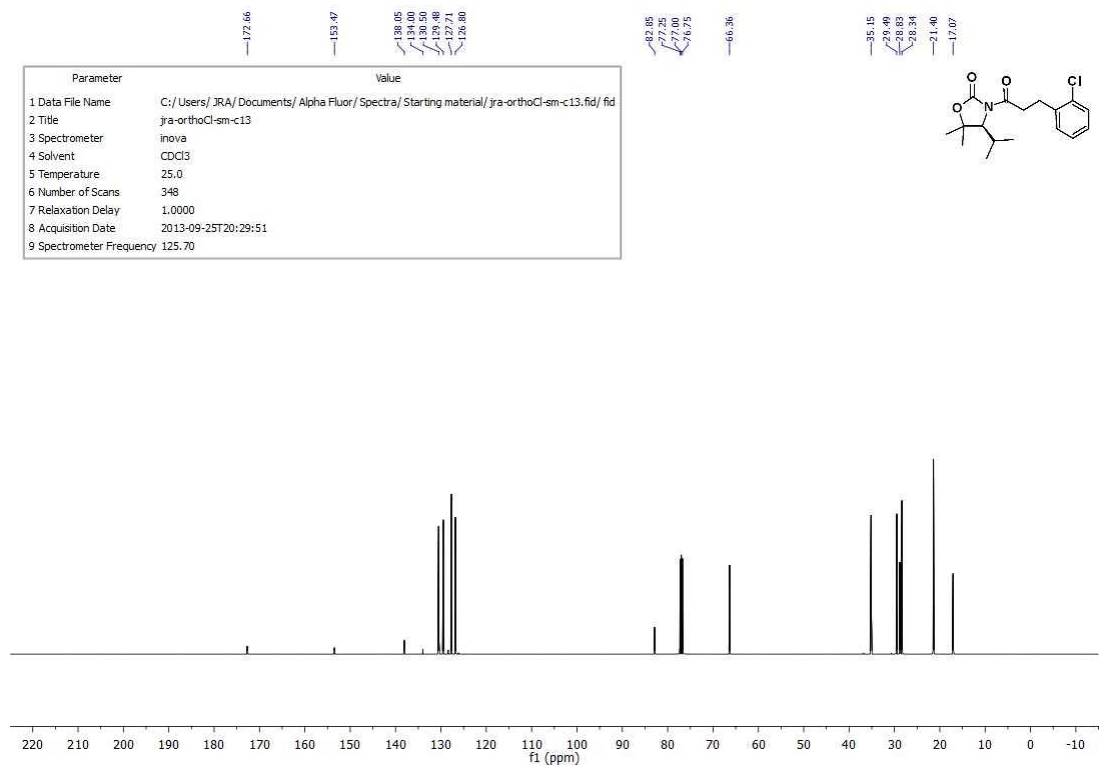
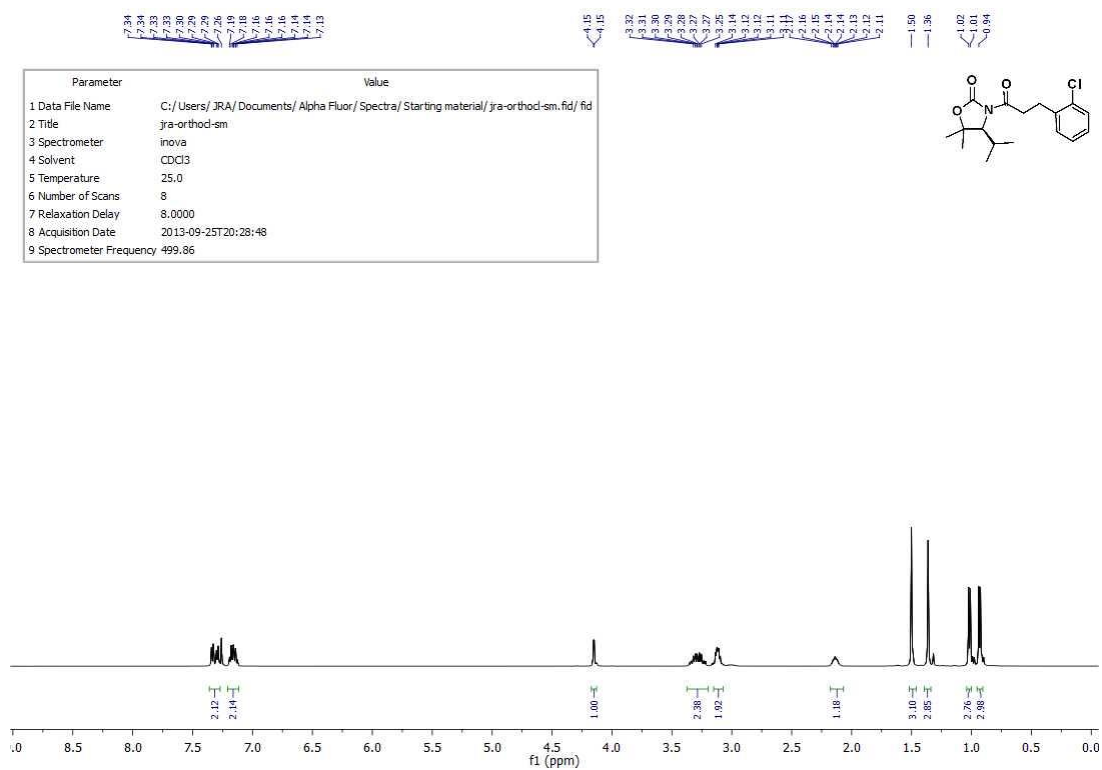
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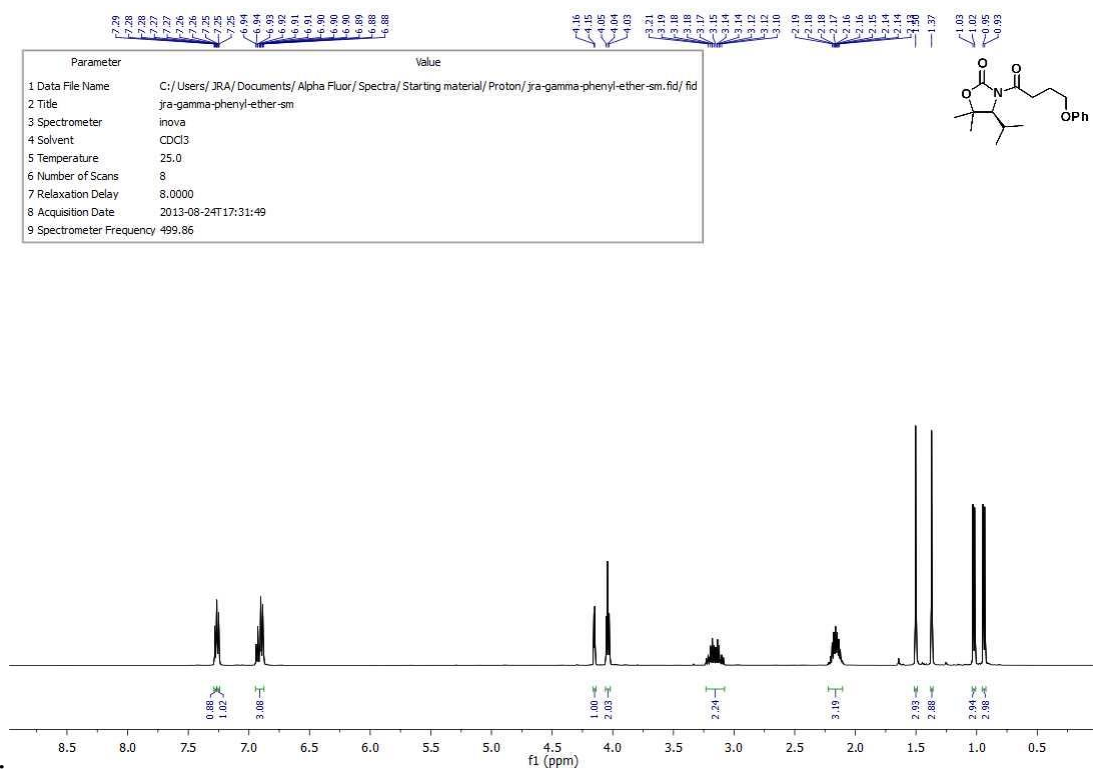


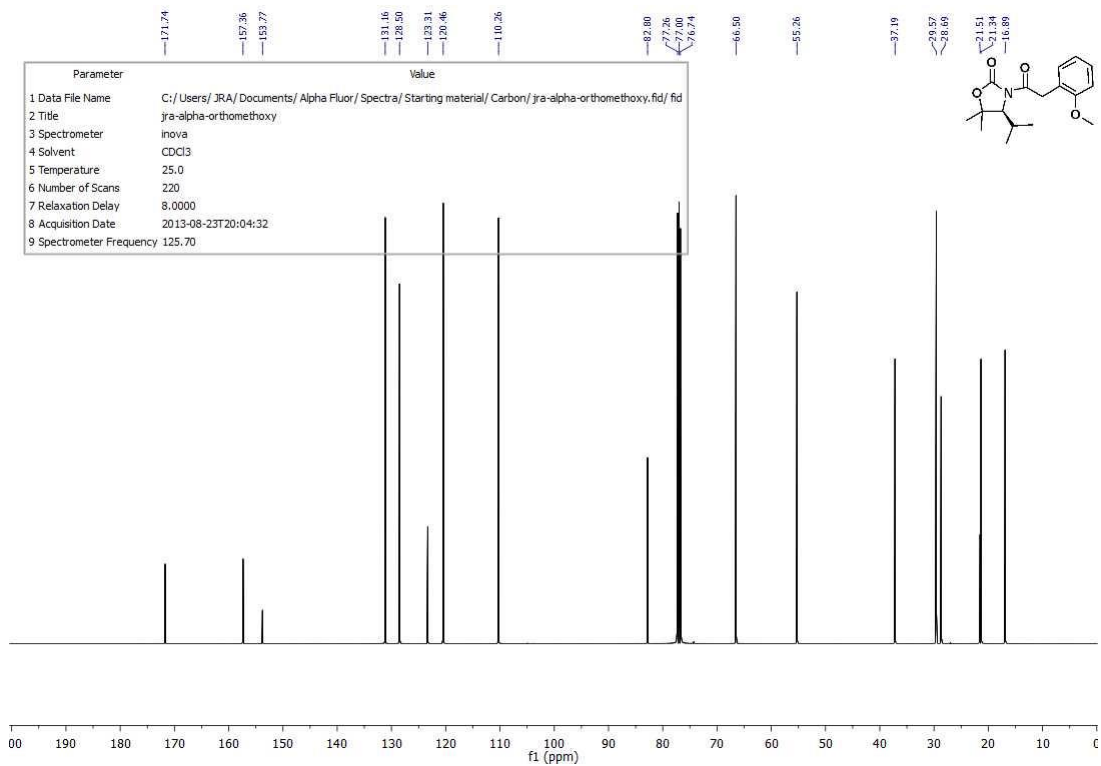
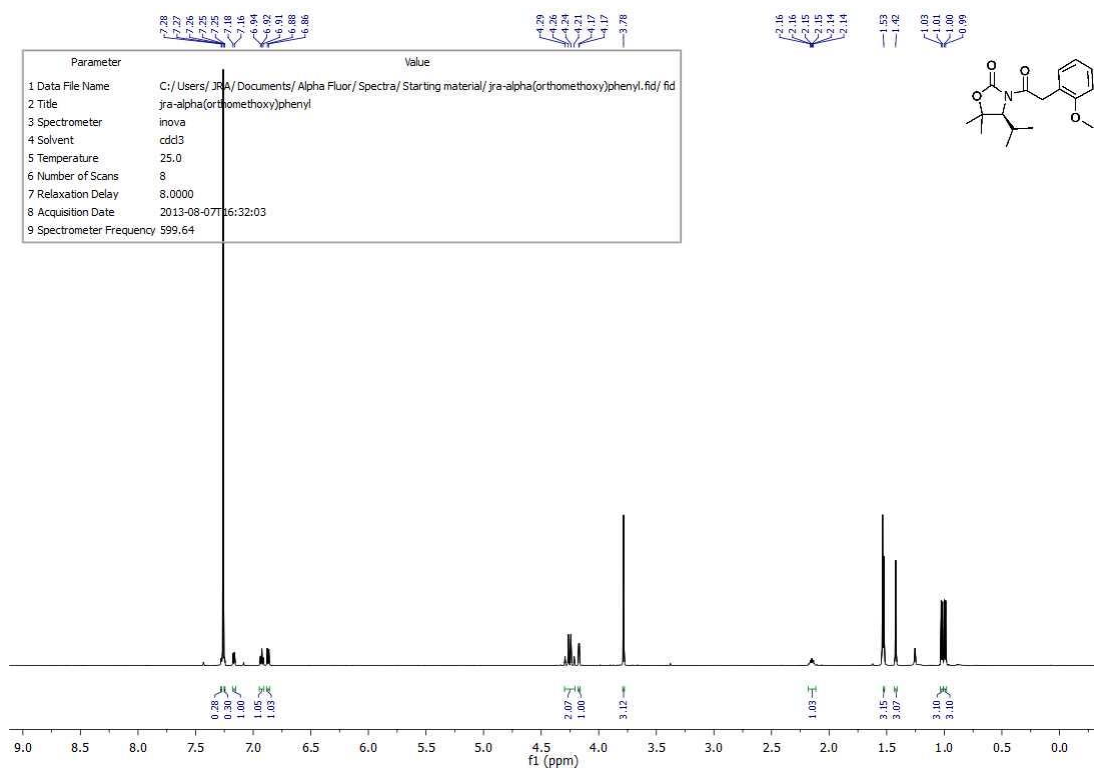


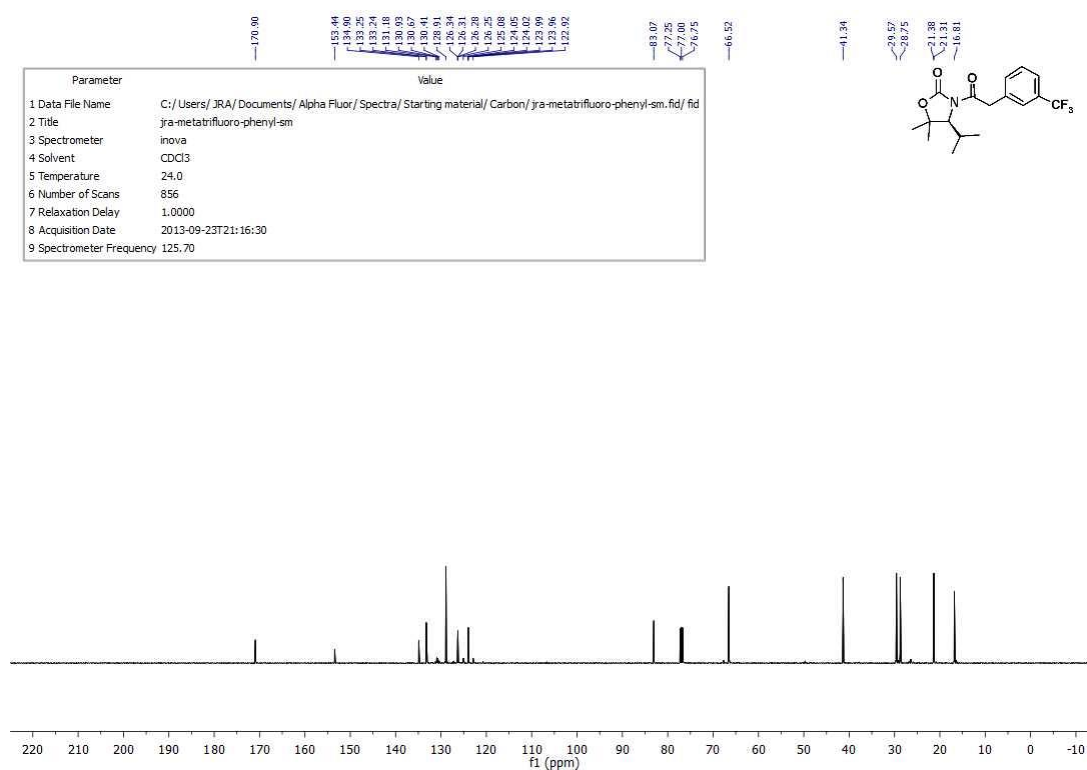
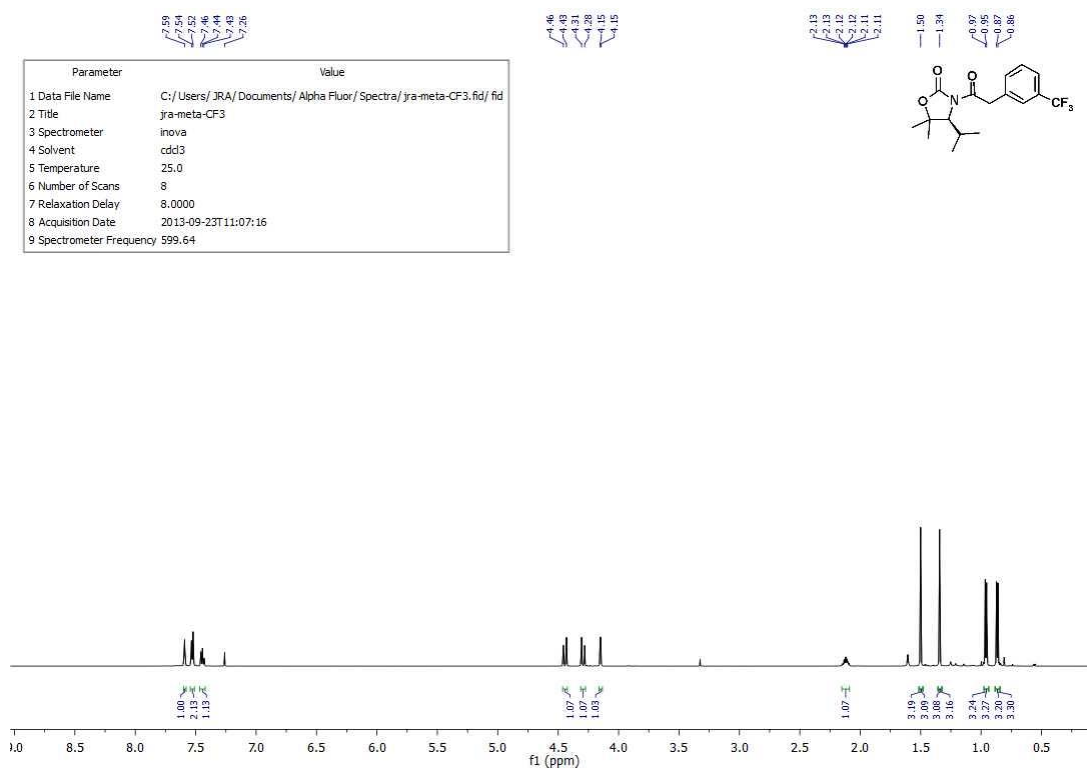


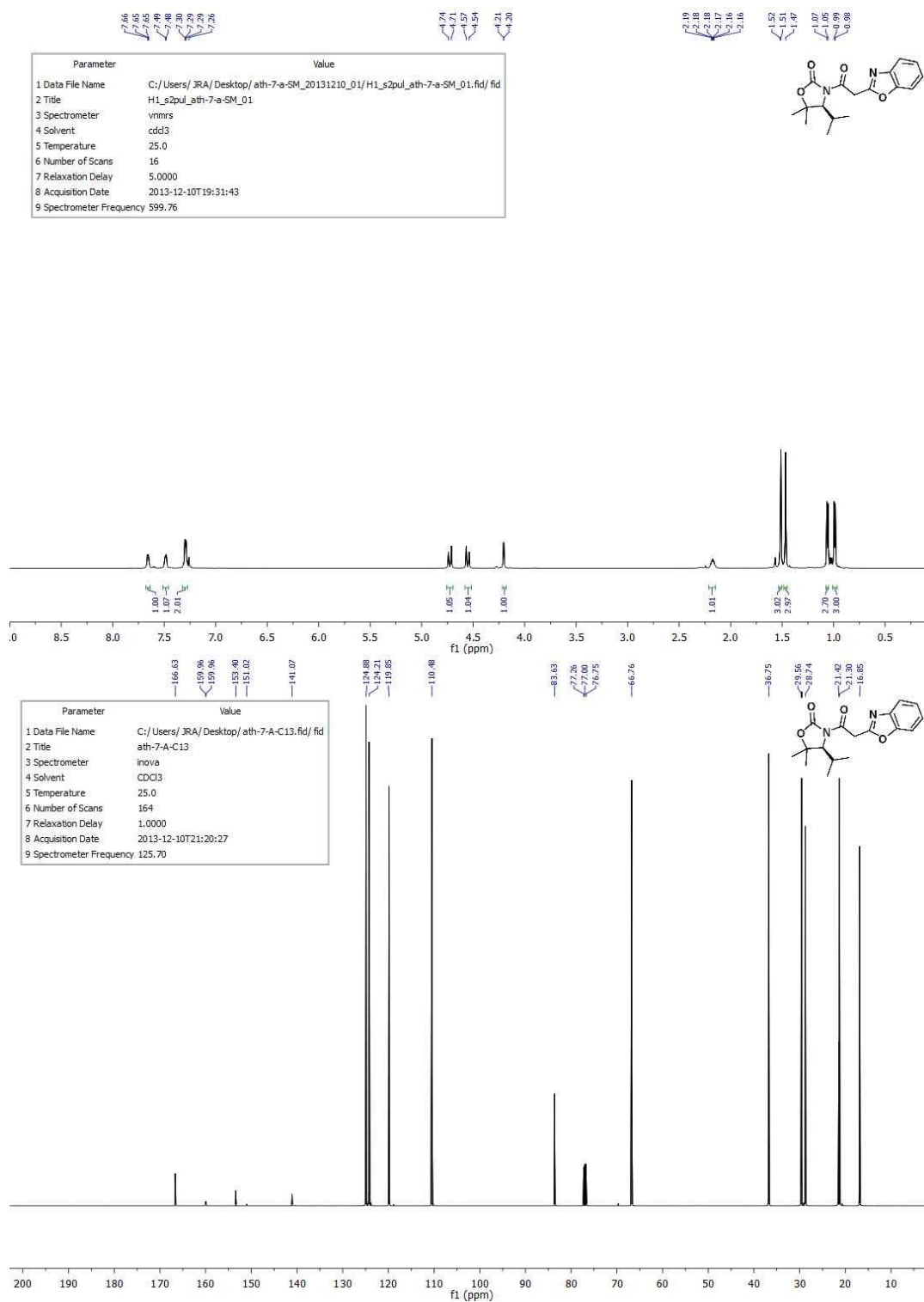


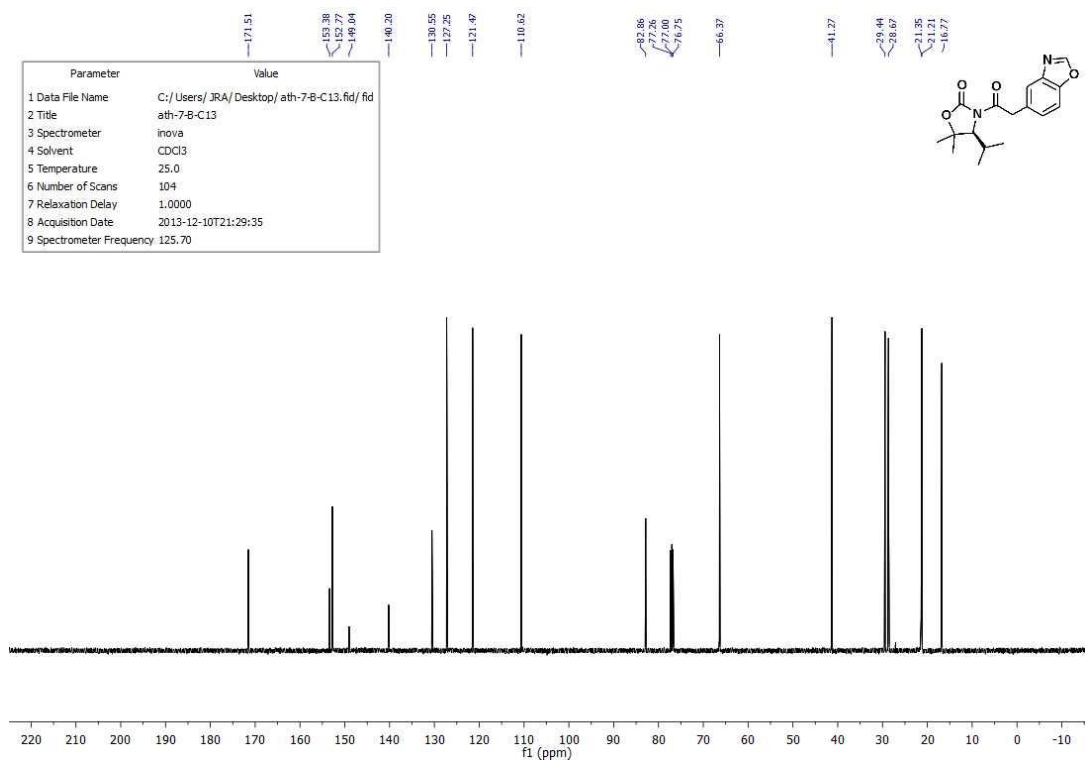
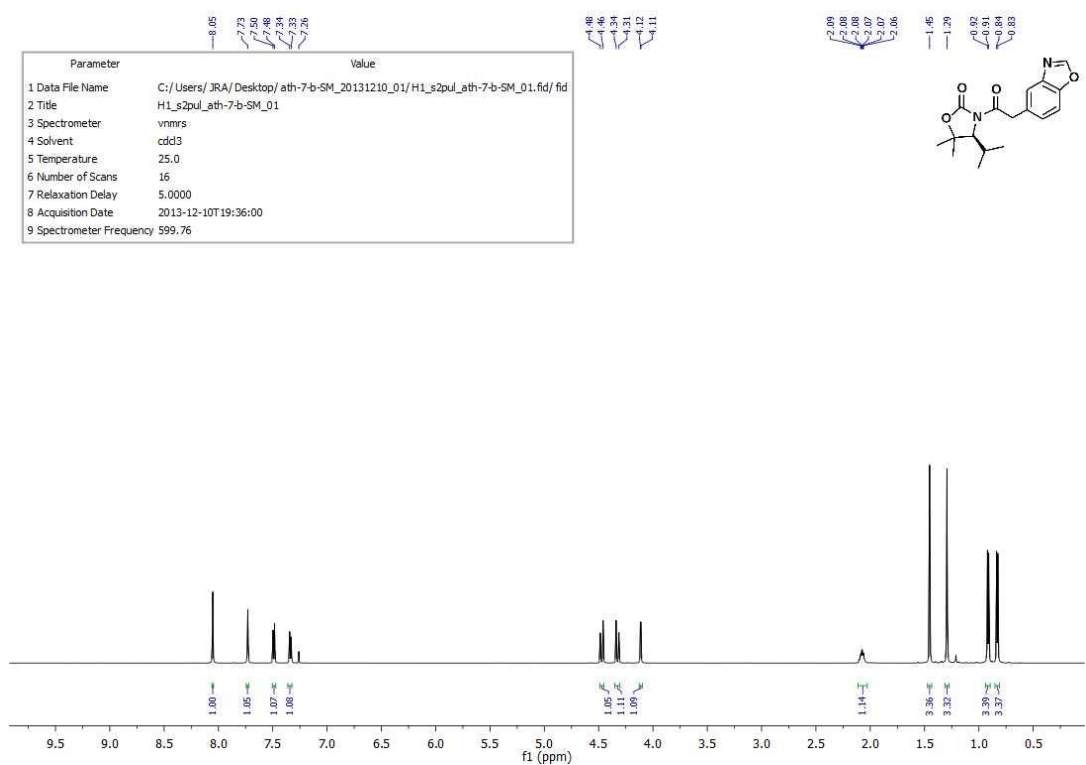


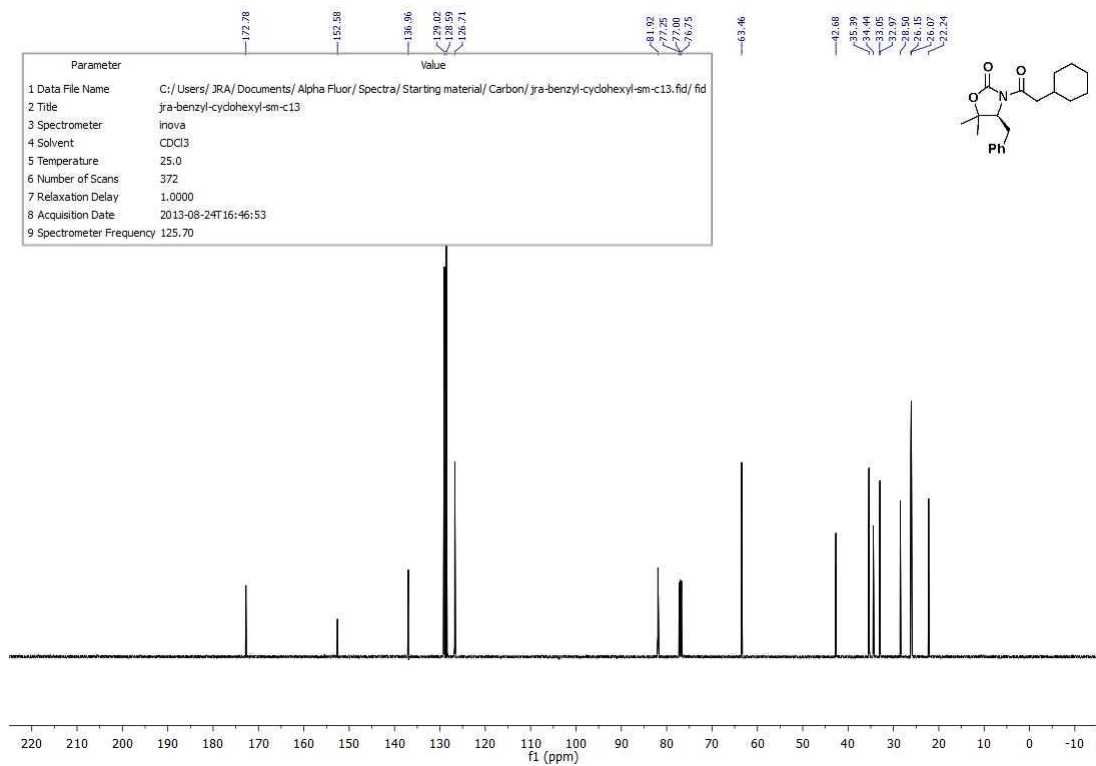
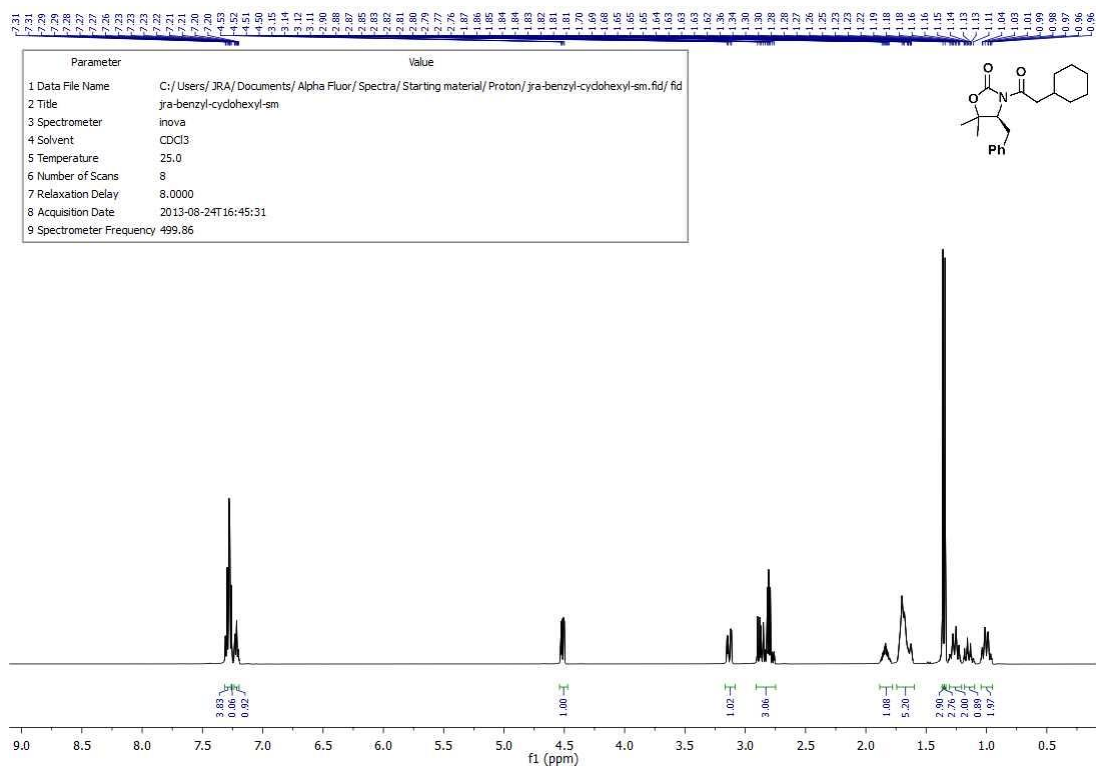


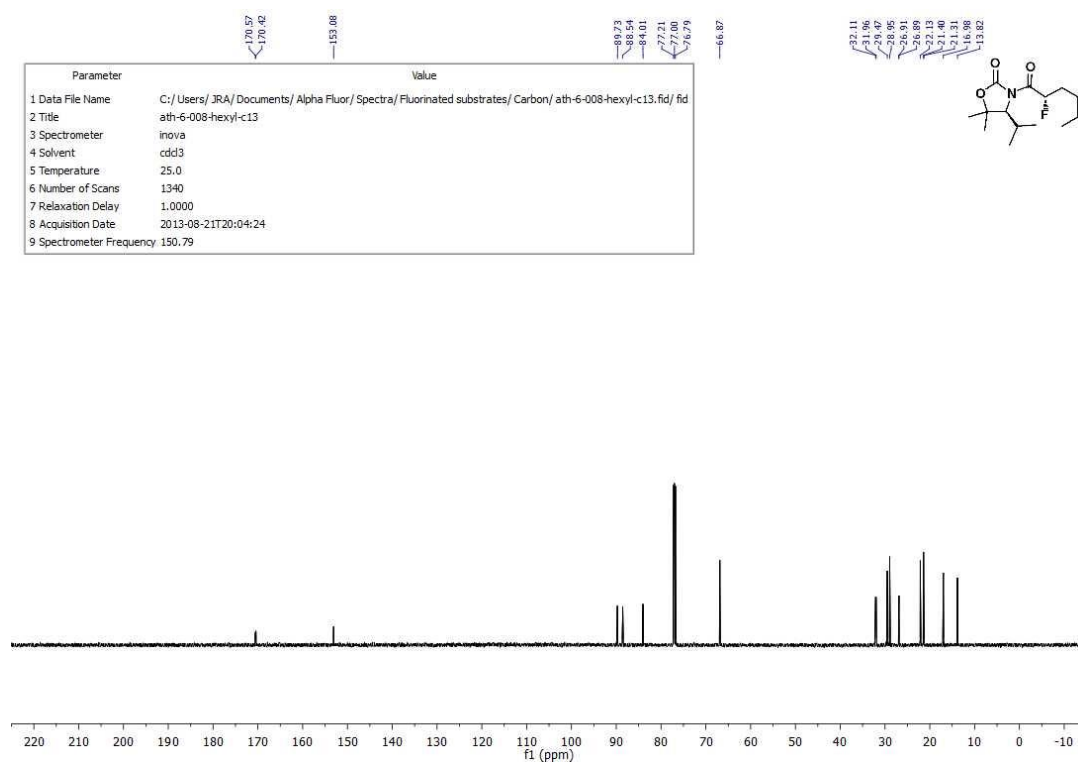
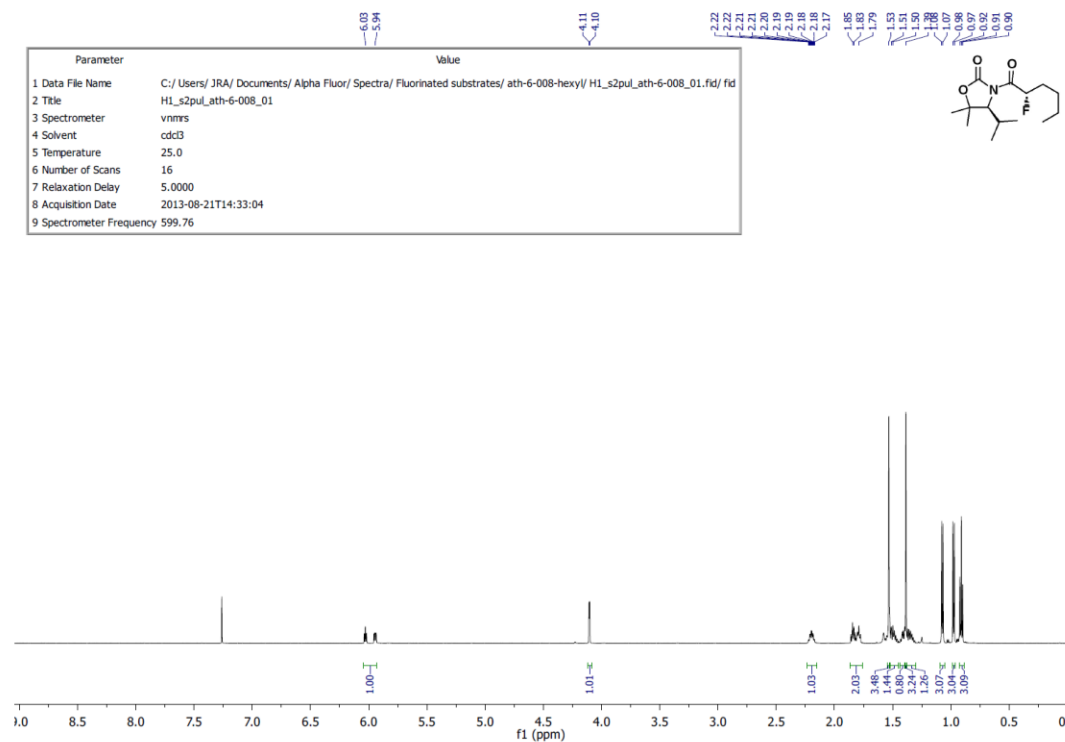


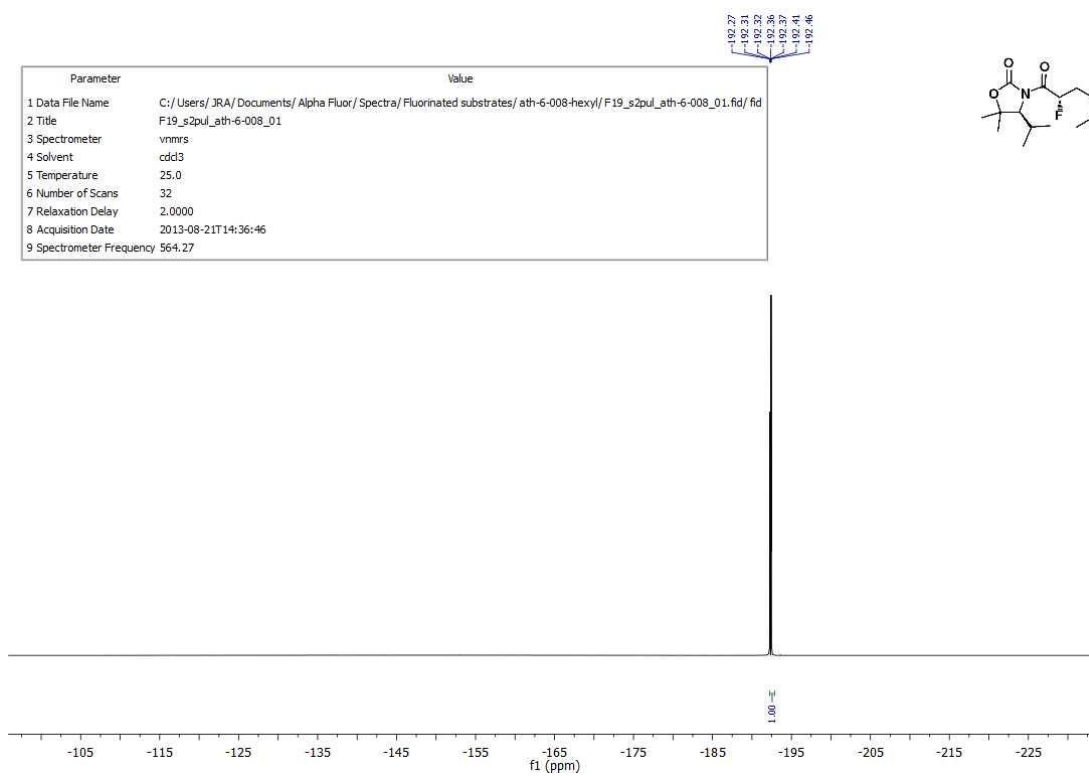


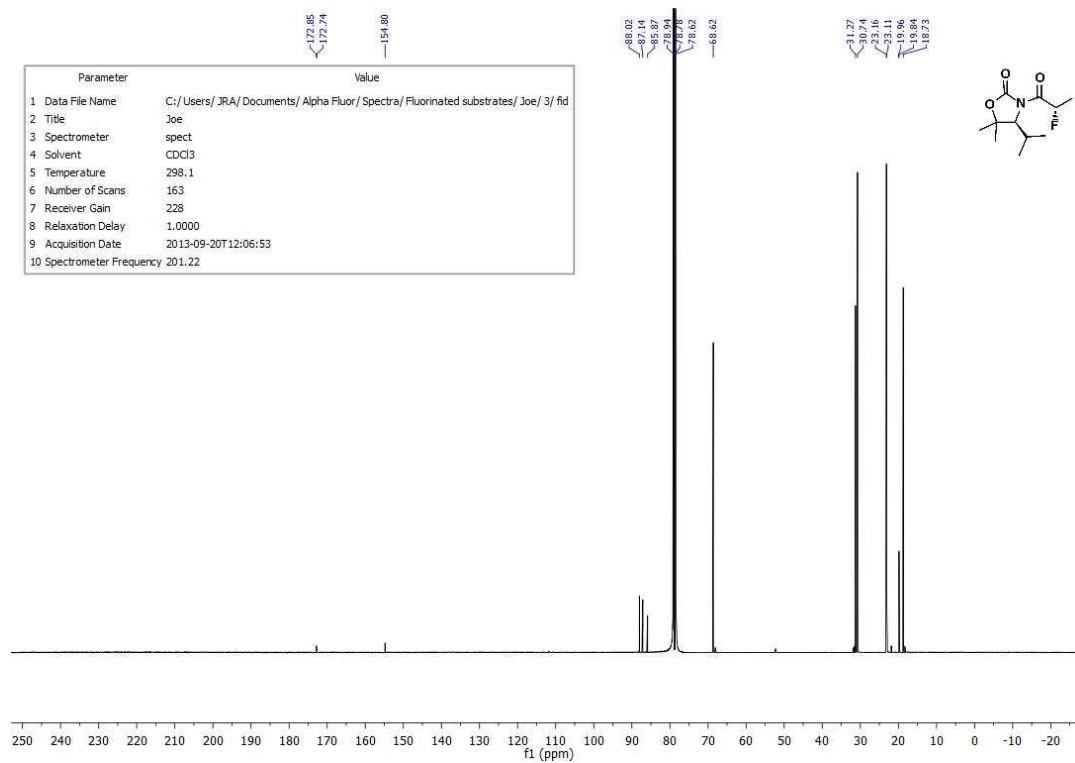
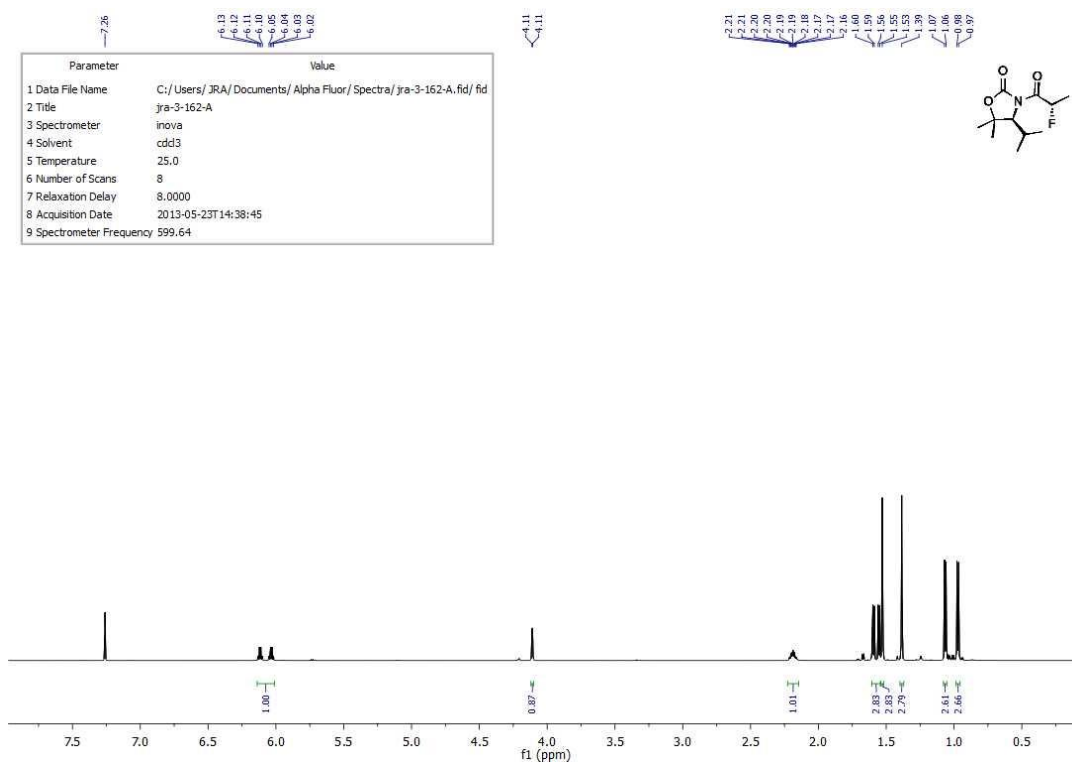


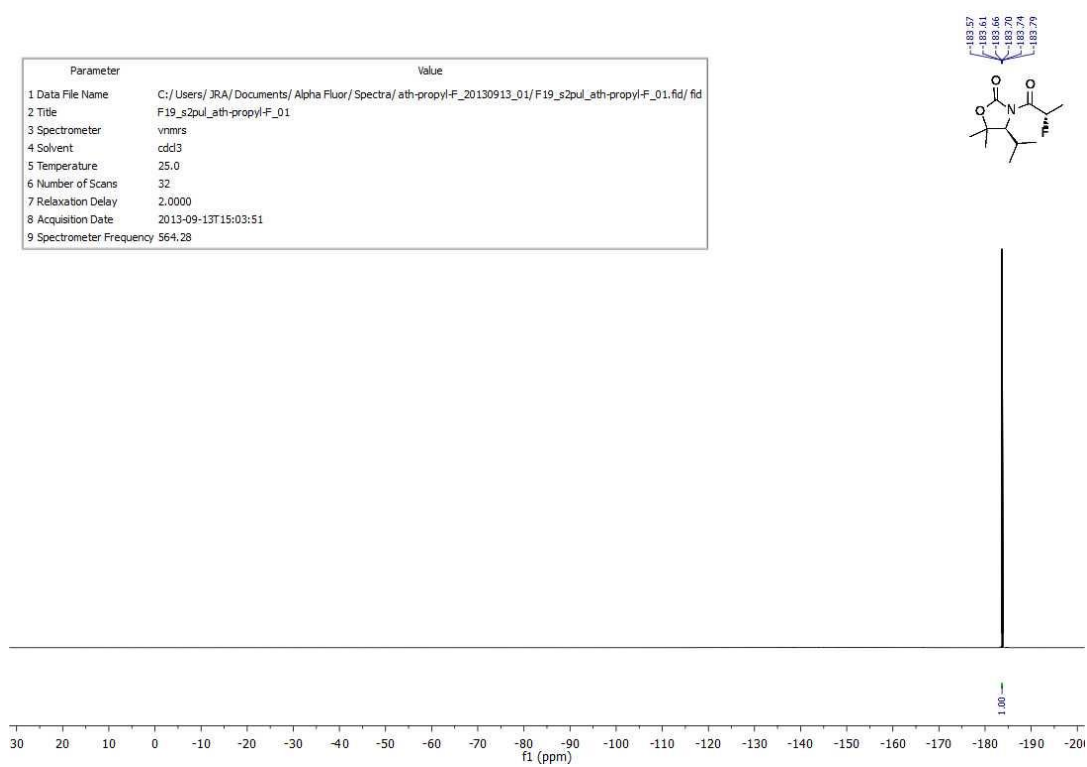


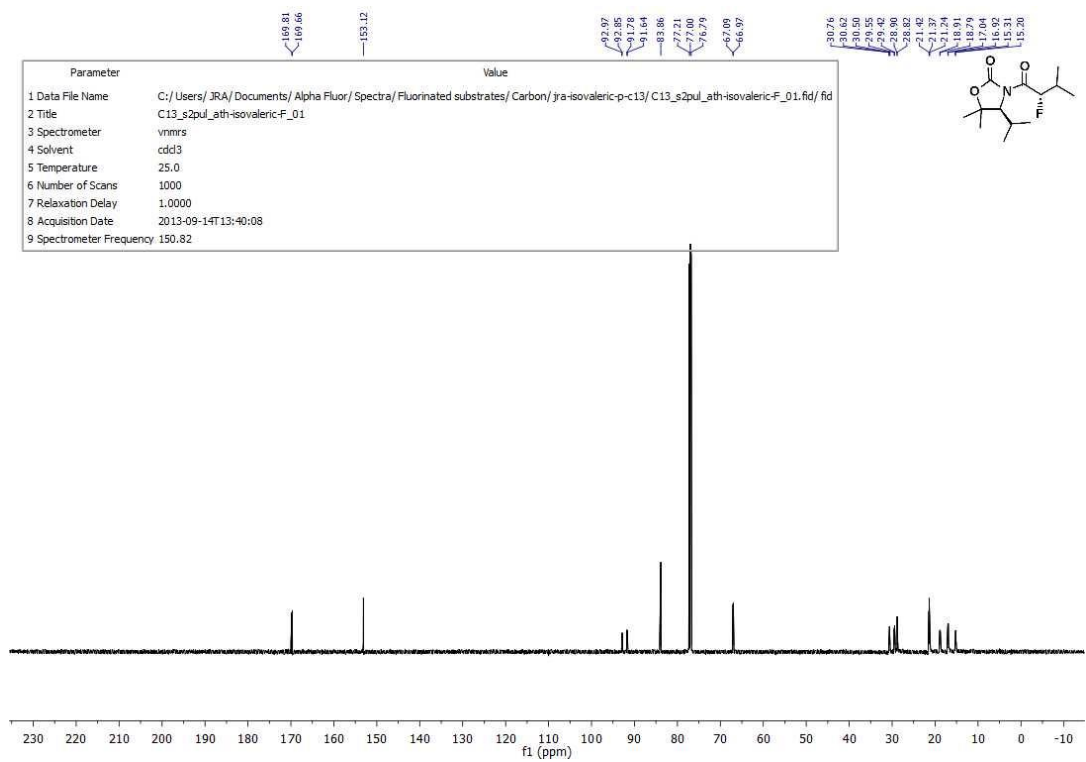
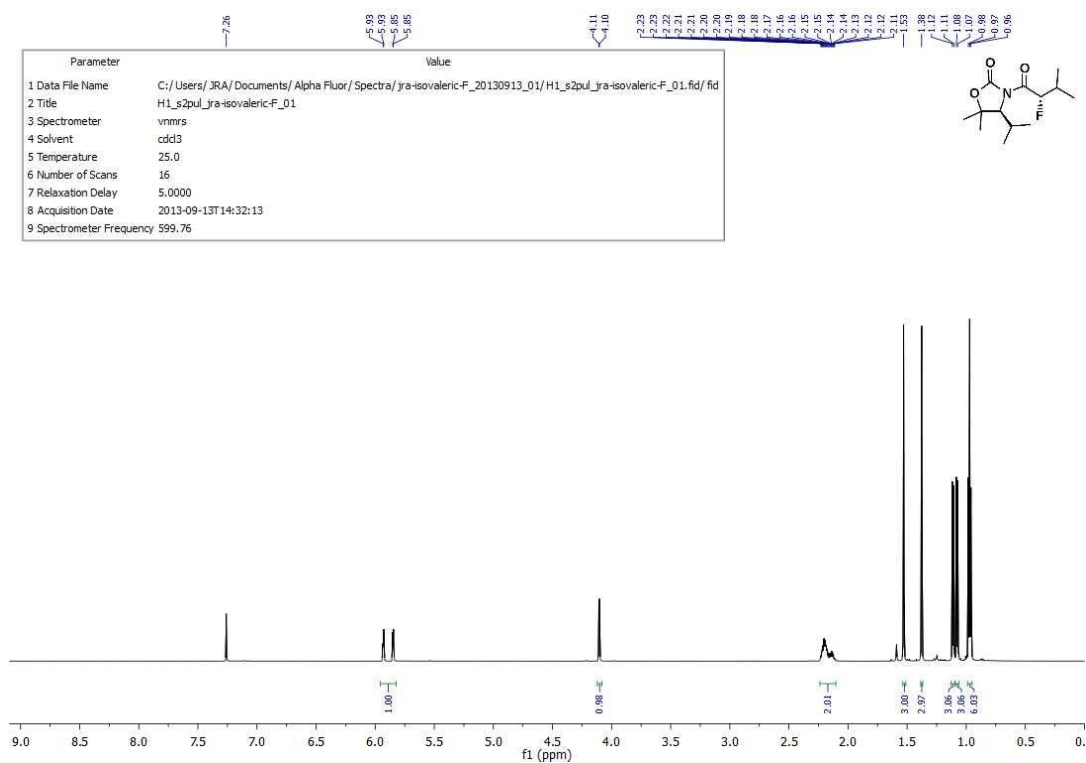


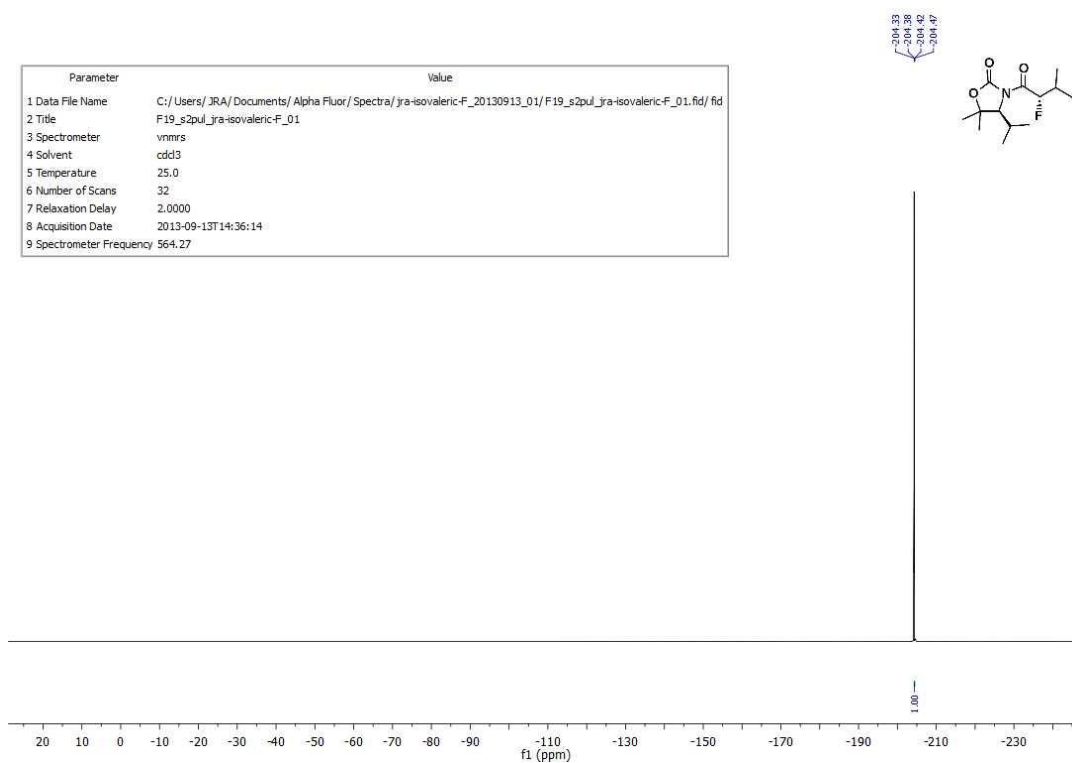


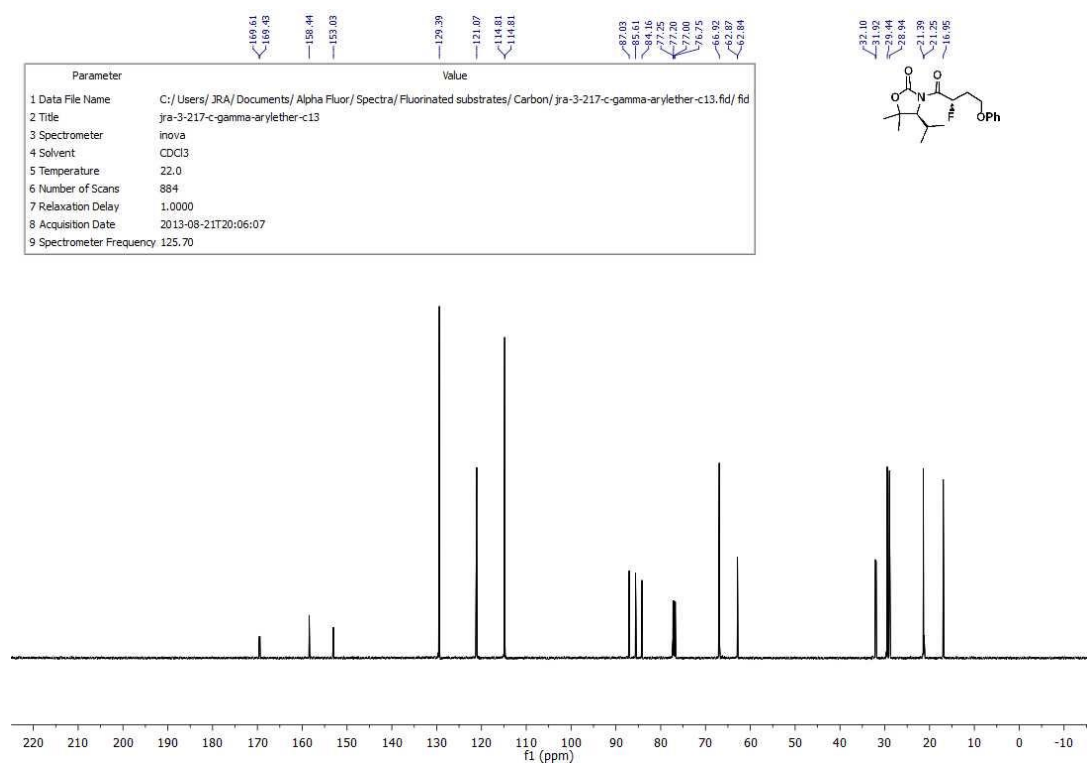
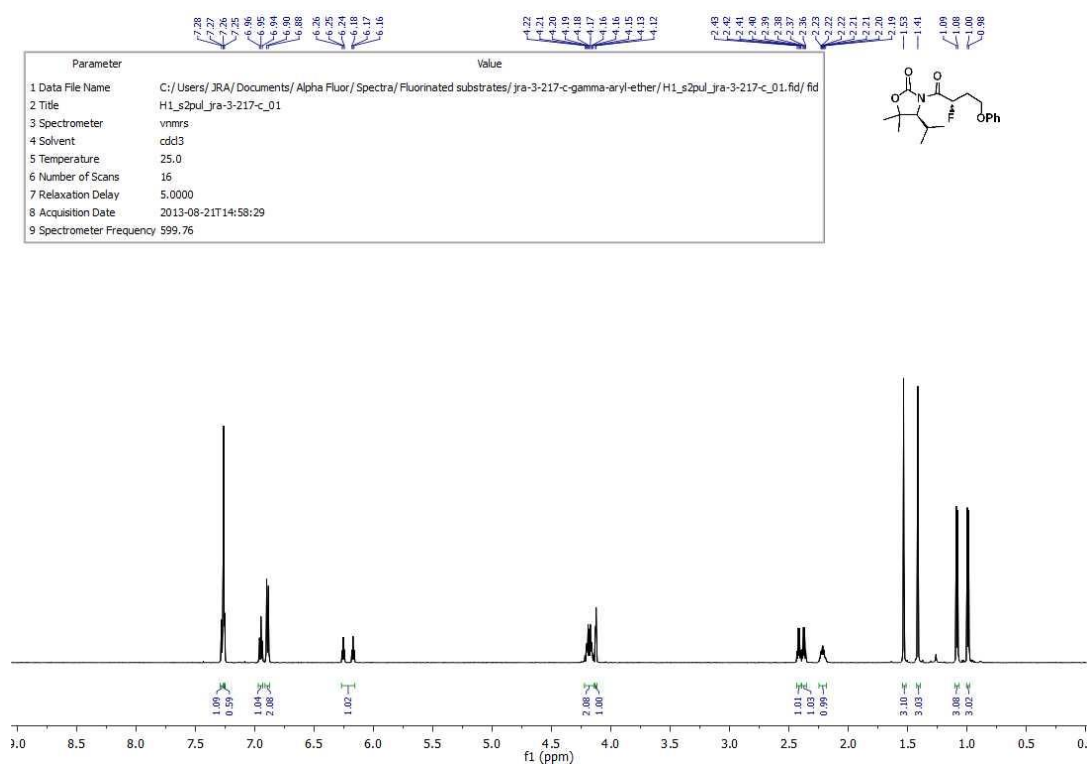


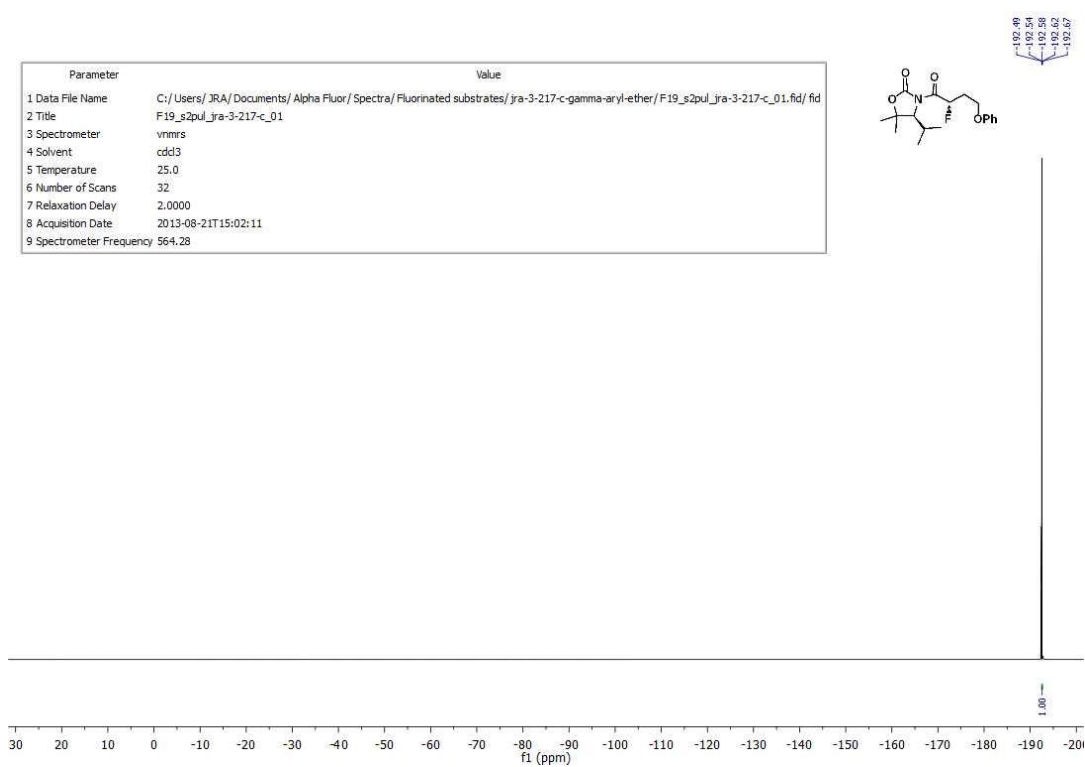


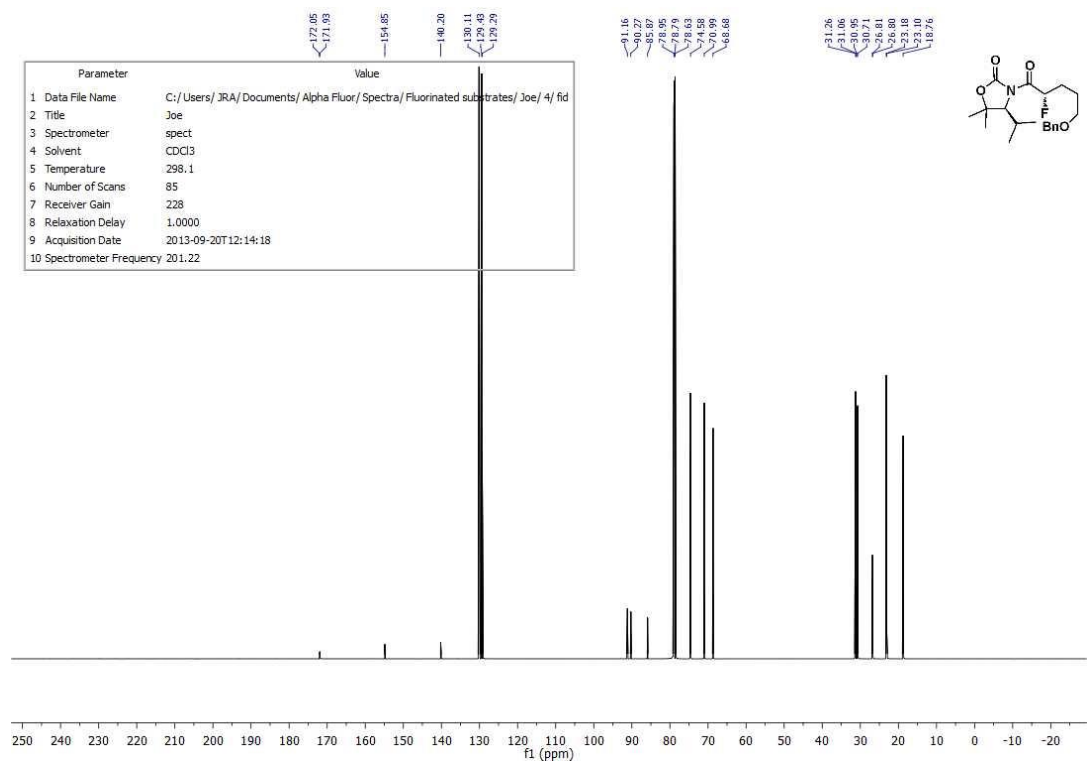
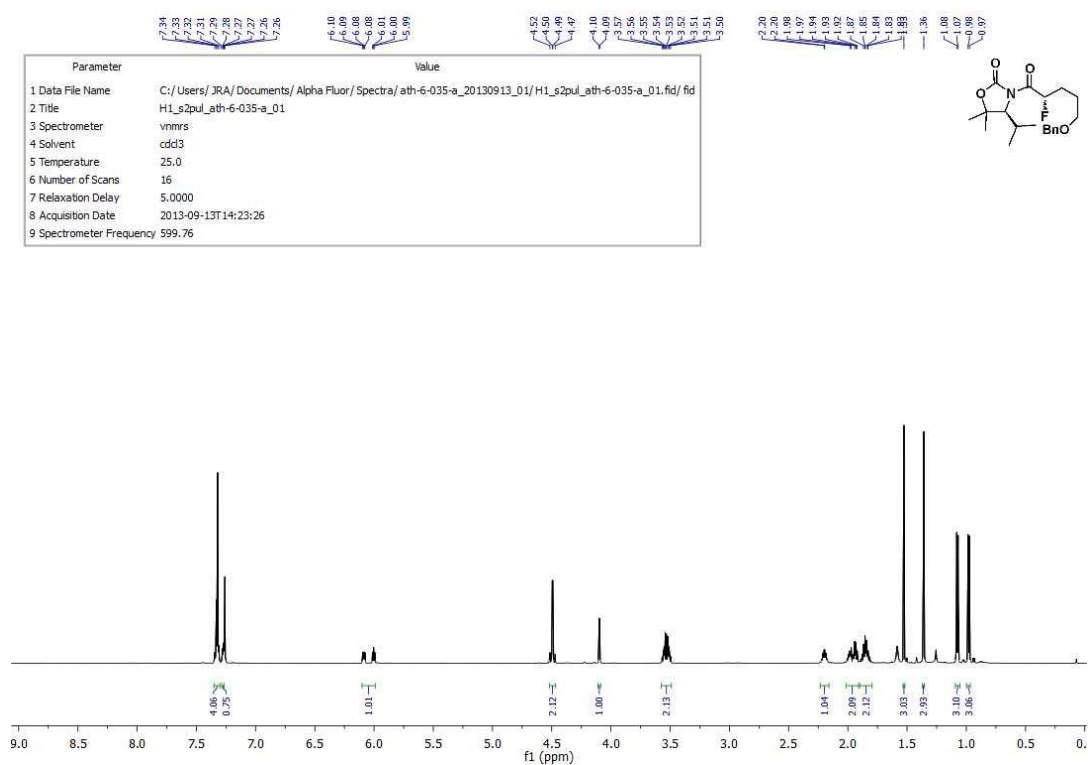






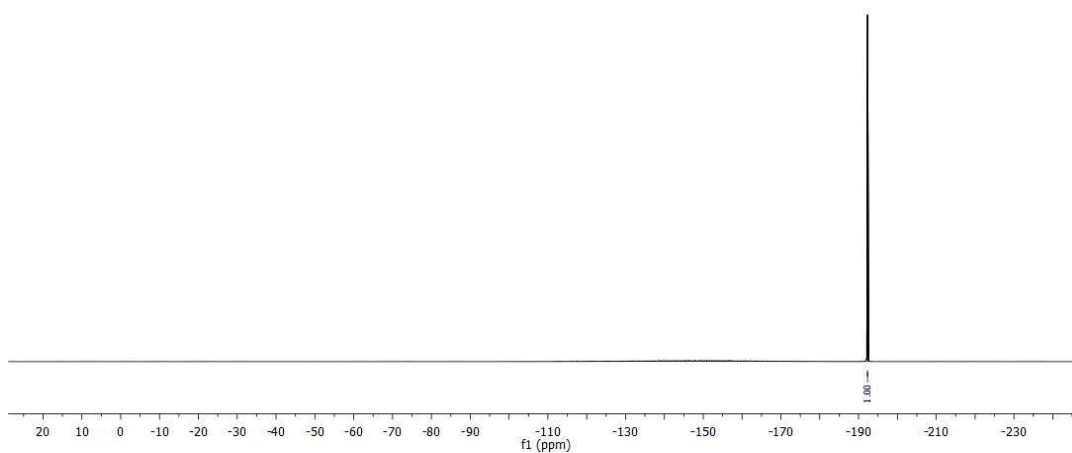
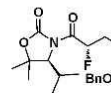


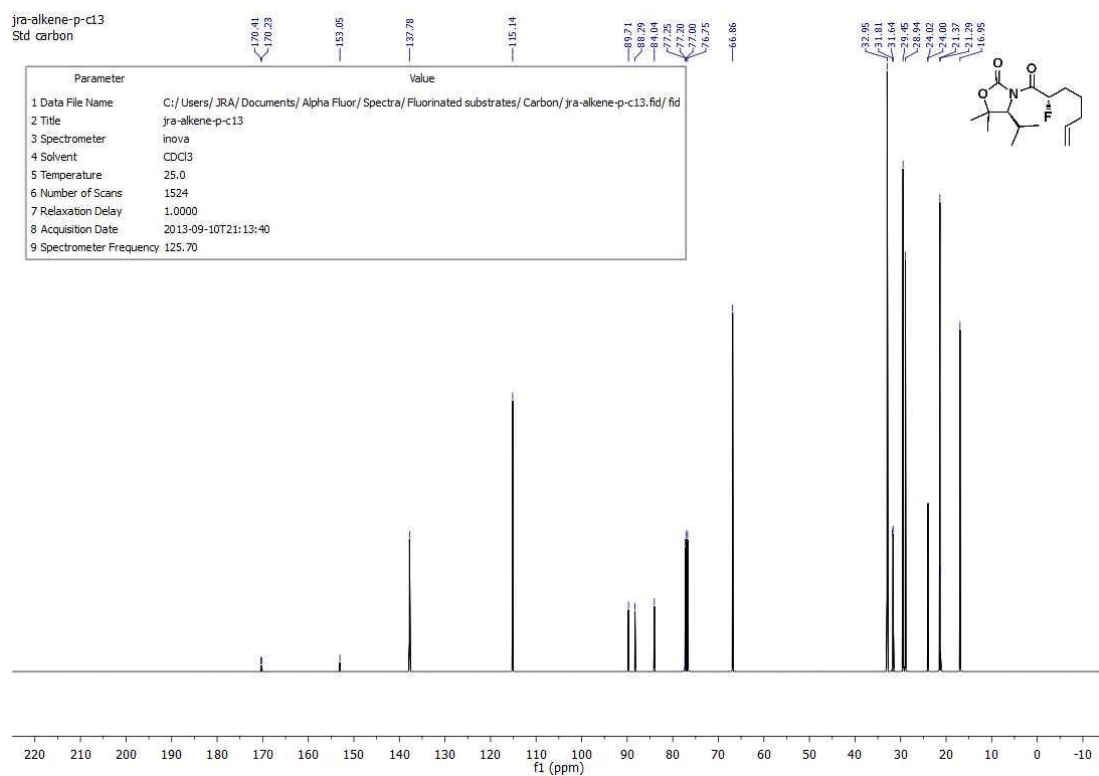
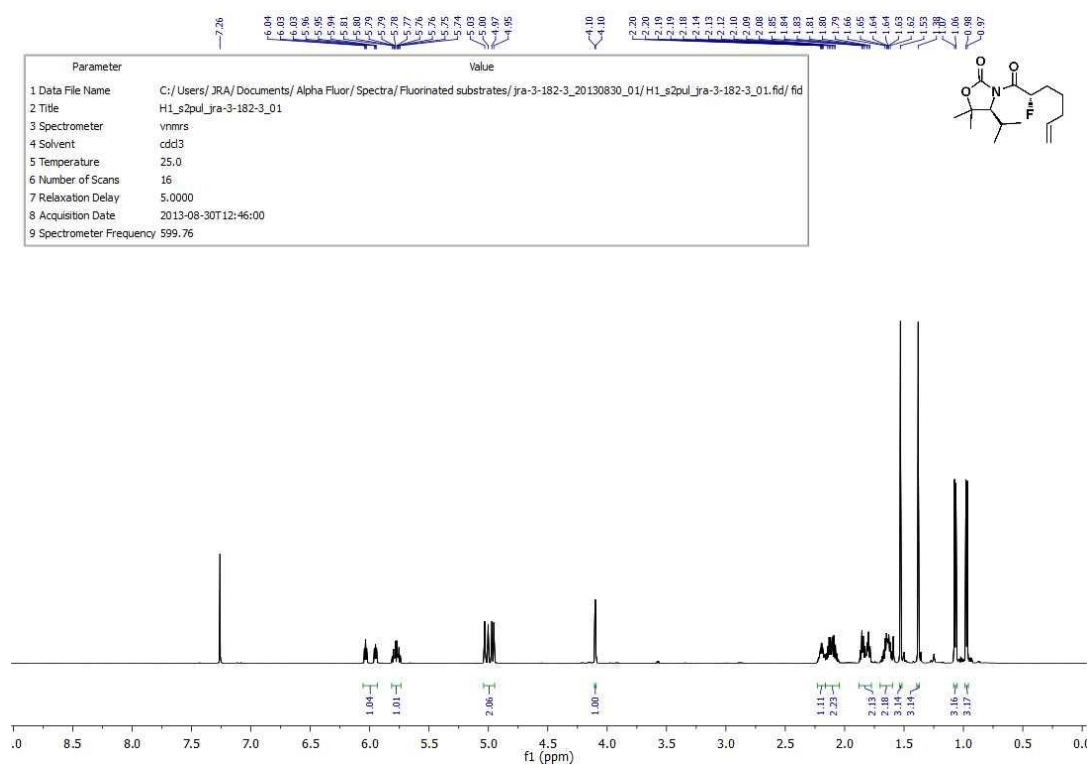




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9 Spectrometer Frequency	564.27

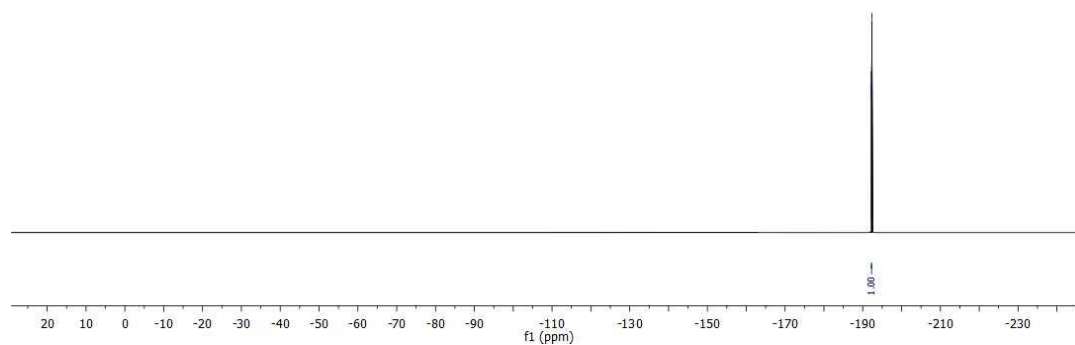
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192.32
192.37
192.41

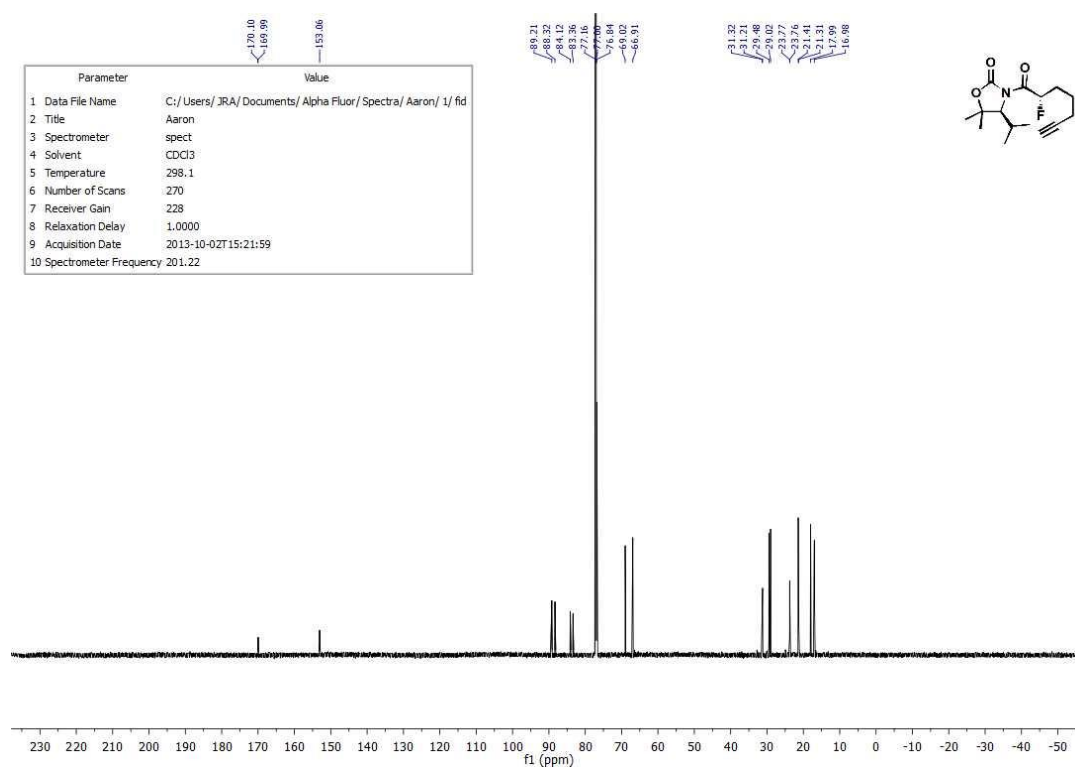
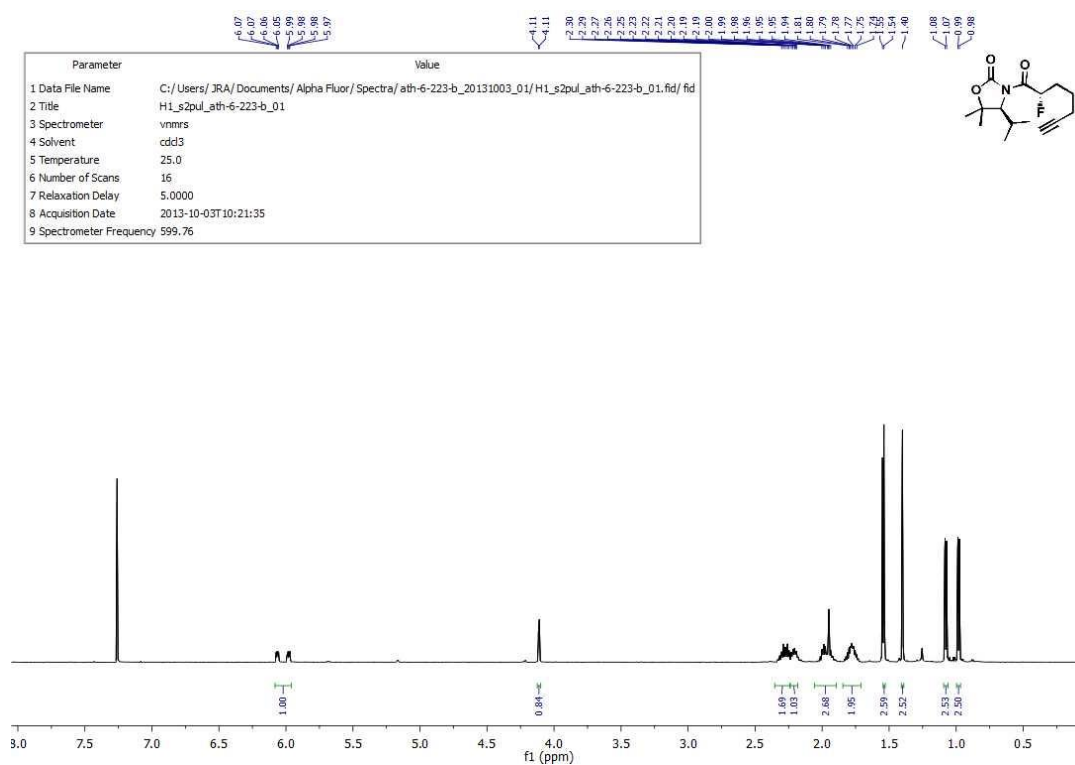




F19_s2pul_jra-3-182-3_01
jra-3-182-3
600MHz

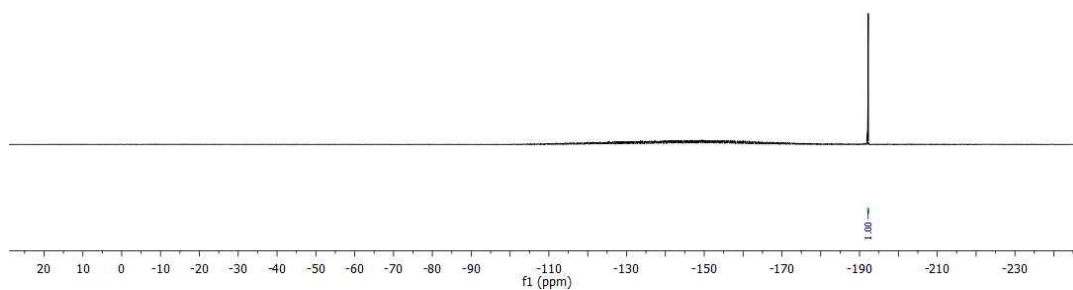
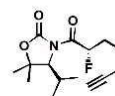
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1 Data File Name	C:/Users/JRA/Documents/Alpha Fluor/Spectra/Fluorinated substrates/jra-3-182-3_20130830_01/F19_s2pul_jra-3-182-3_01.fid/ fid
2 Title	F19_s2pul_jra-3-182-3_01
3 Spectrometer	nmrns
4 Solvent	cdcl3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-08-30T12:49:19
9 Spectrometer Frequency	564.27

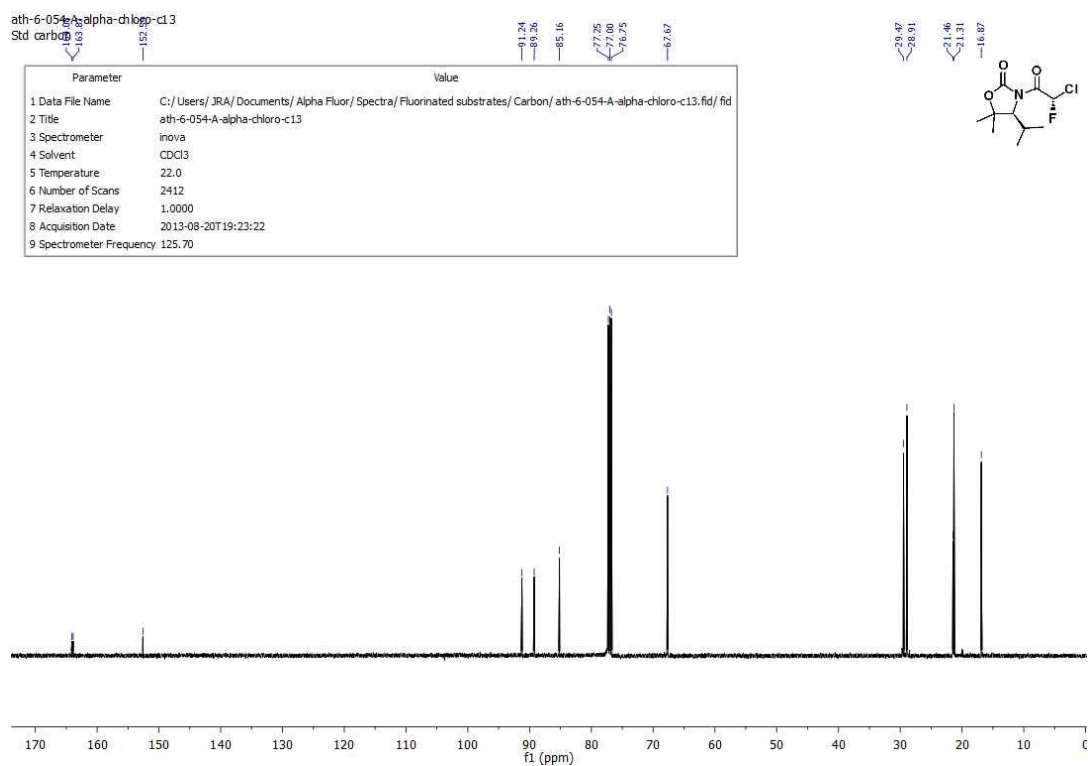
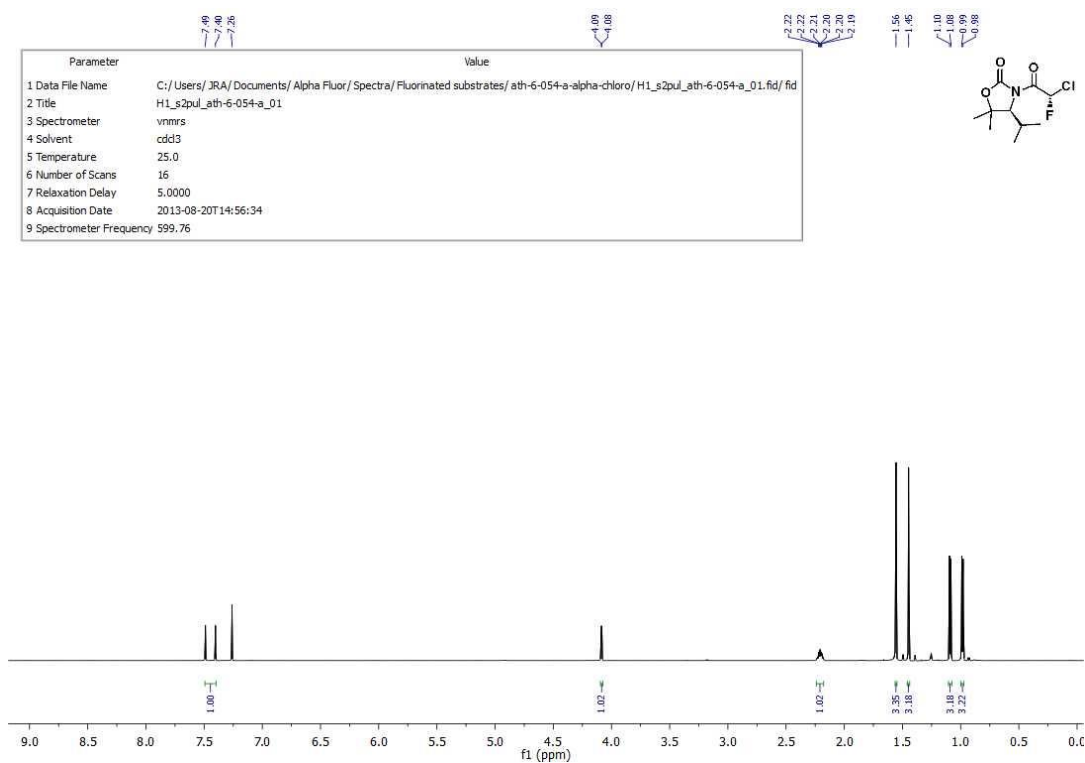




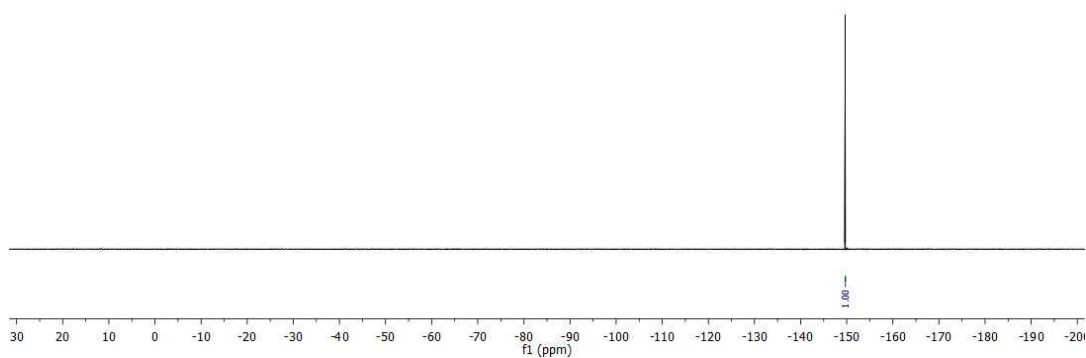
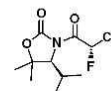
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1 Data File Name	C:/Users/JRA/Documents/Alpha Fluor/Spectra/ath-6-223-b_20131003_01/F19_s2pul_ath-6-223-b_01.fid/fid
2 Title	F19_s2pul_ath-6-223-b_01
3 Spectrometer	nmrns
4 Solvent	cdd3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-10-03T10:25:03
9 Spectrometer Frequency	564.27

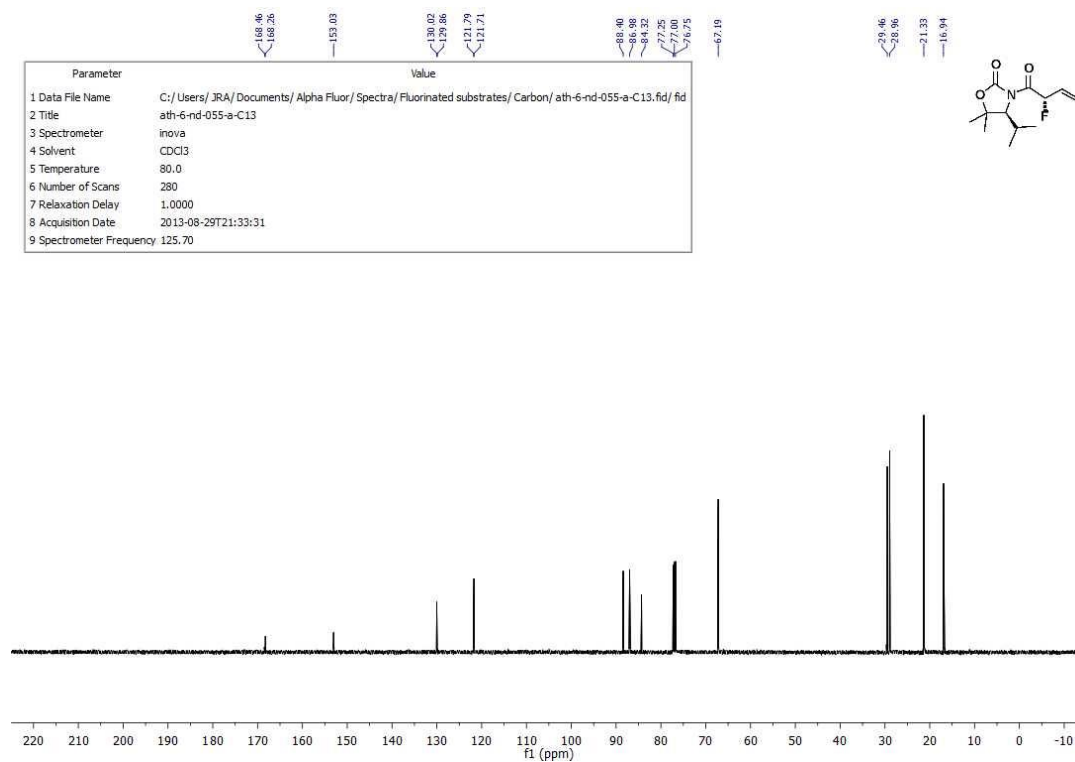
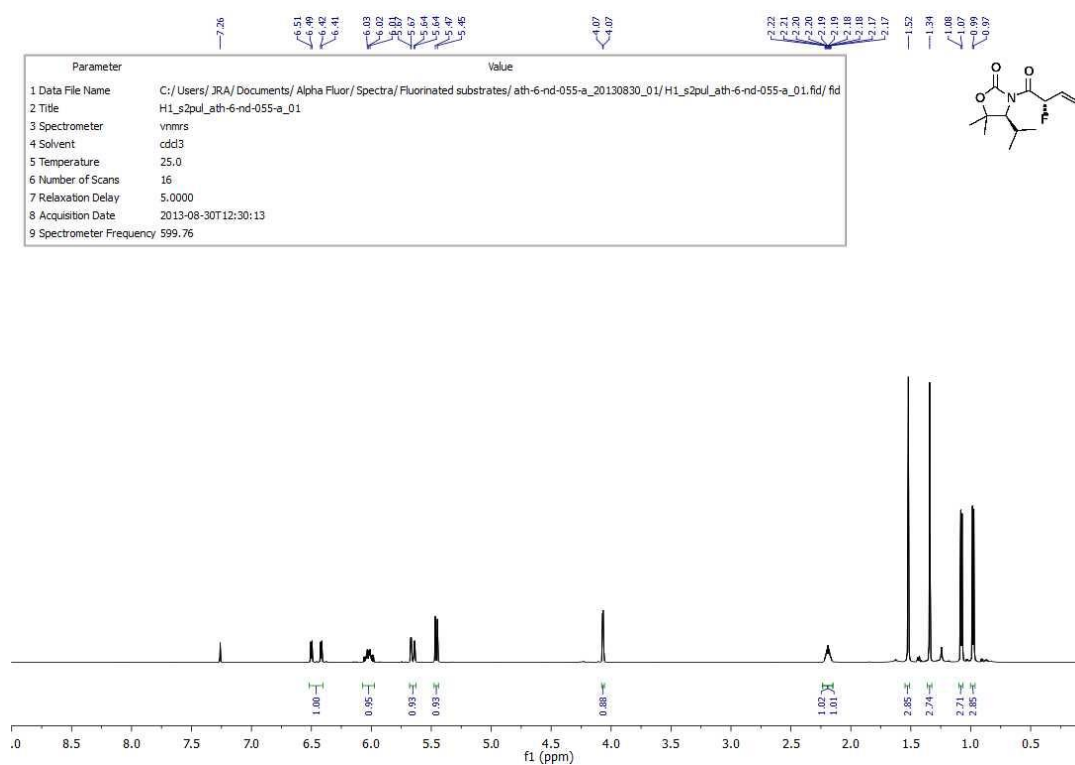
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192.26
192.30

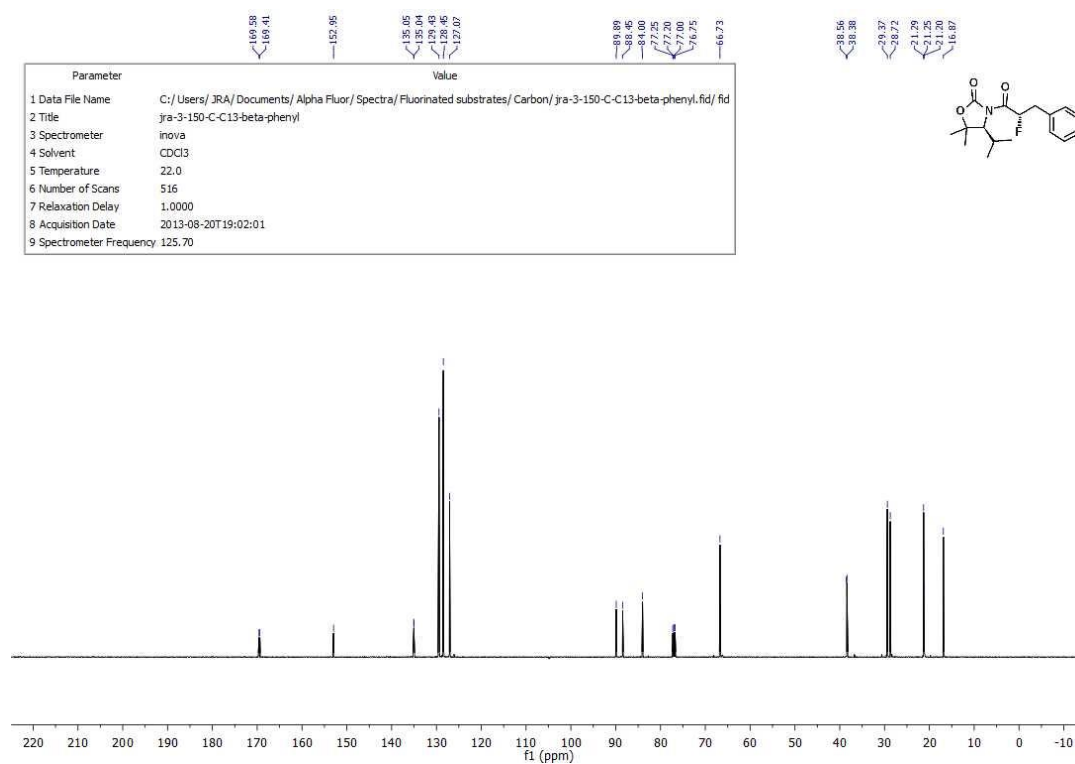
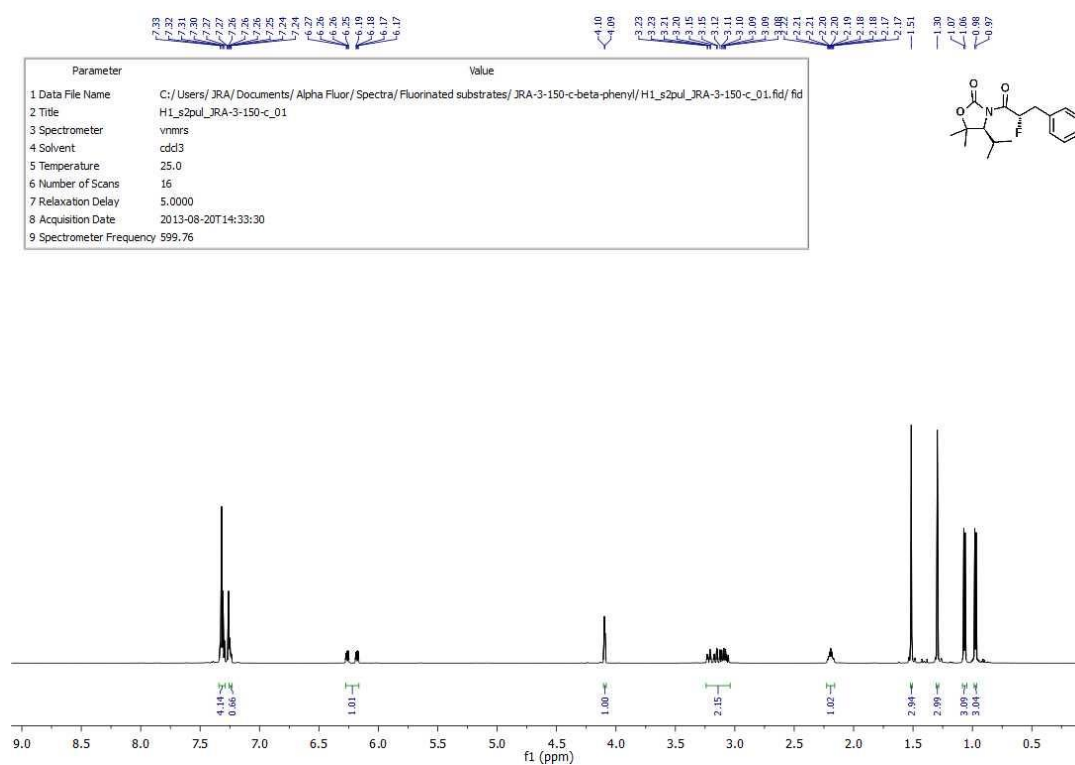


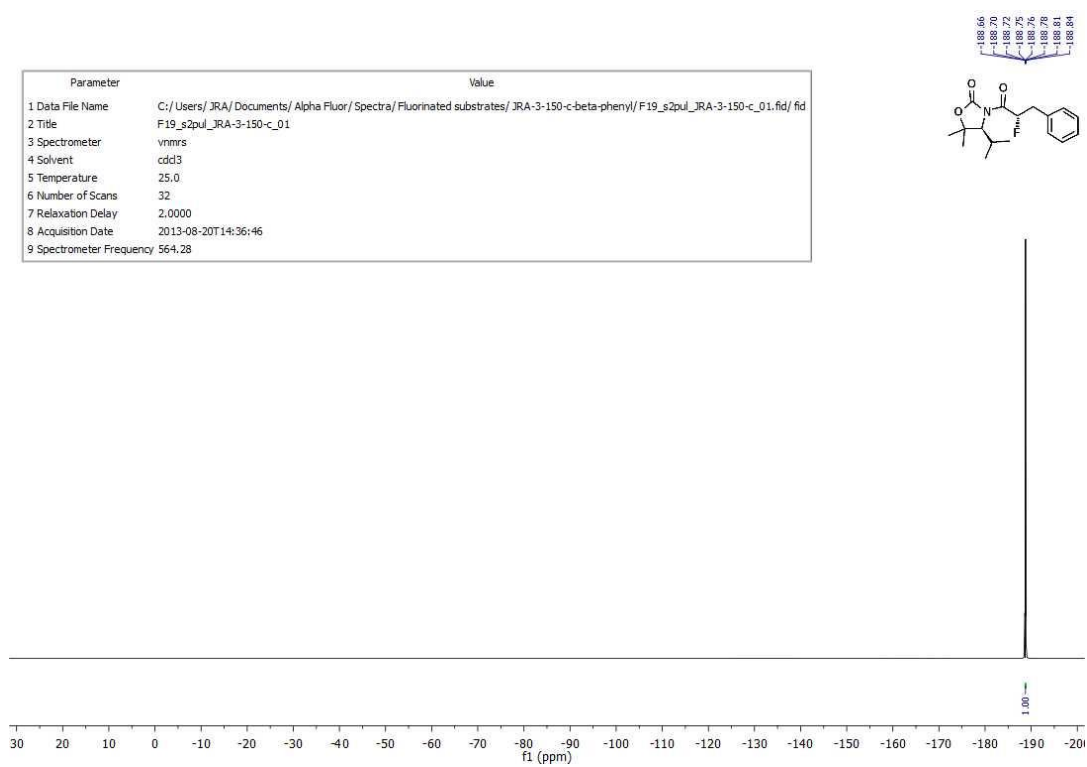


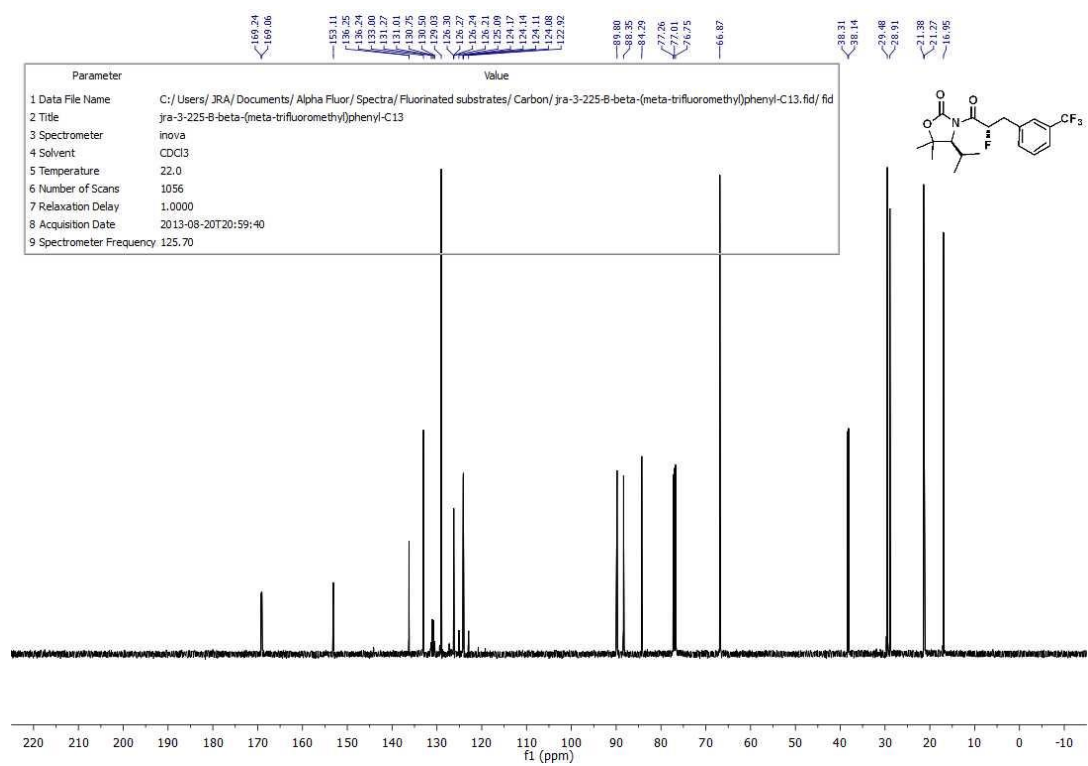
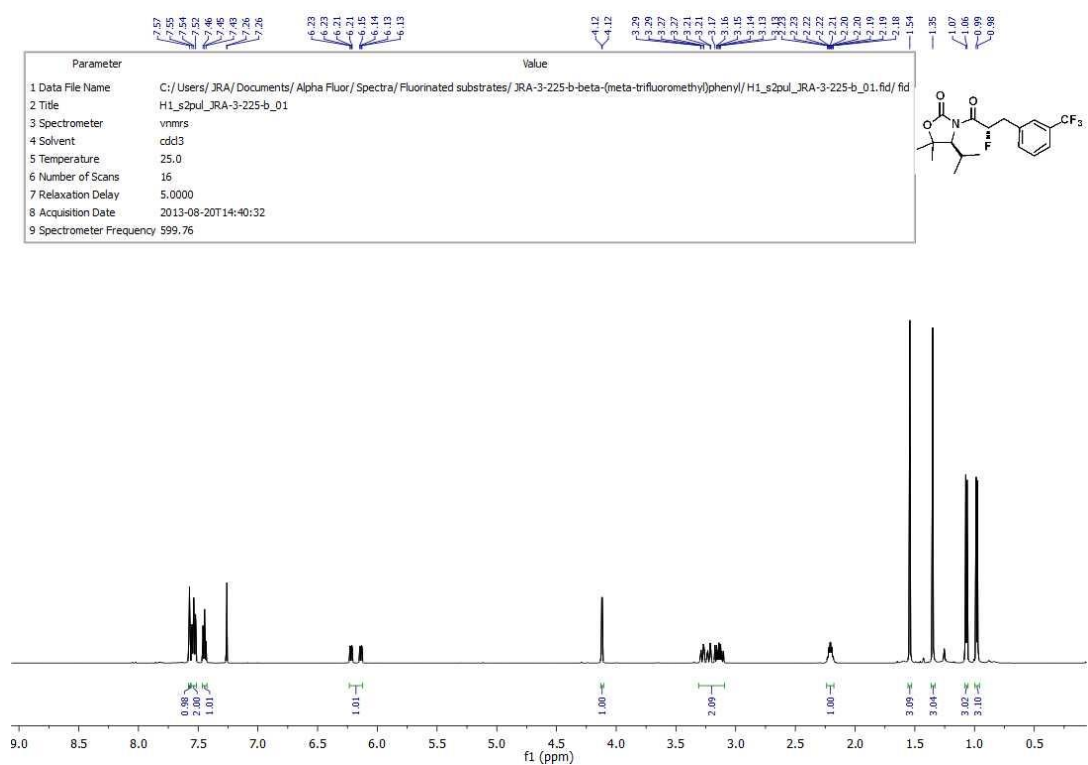
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1 Data File Name	C:/Users/JRA/Documents/Alpha Fluor/ Spectra/ Fluorinated substrates/ ath-6-054-a-alpha-chloro/ F19_s2pul_ath-6-054-a_01.fid/ fid
2 Title	F19_s2pul_ath-6-054-a_01
3 Spectrometer	vmnms
4 Solvent	cdcl3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-08-20T14:59:55
9 Spectrometer Frequency	564.28

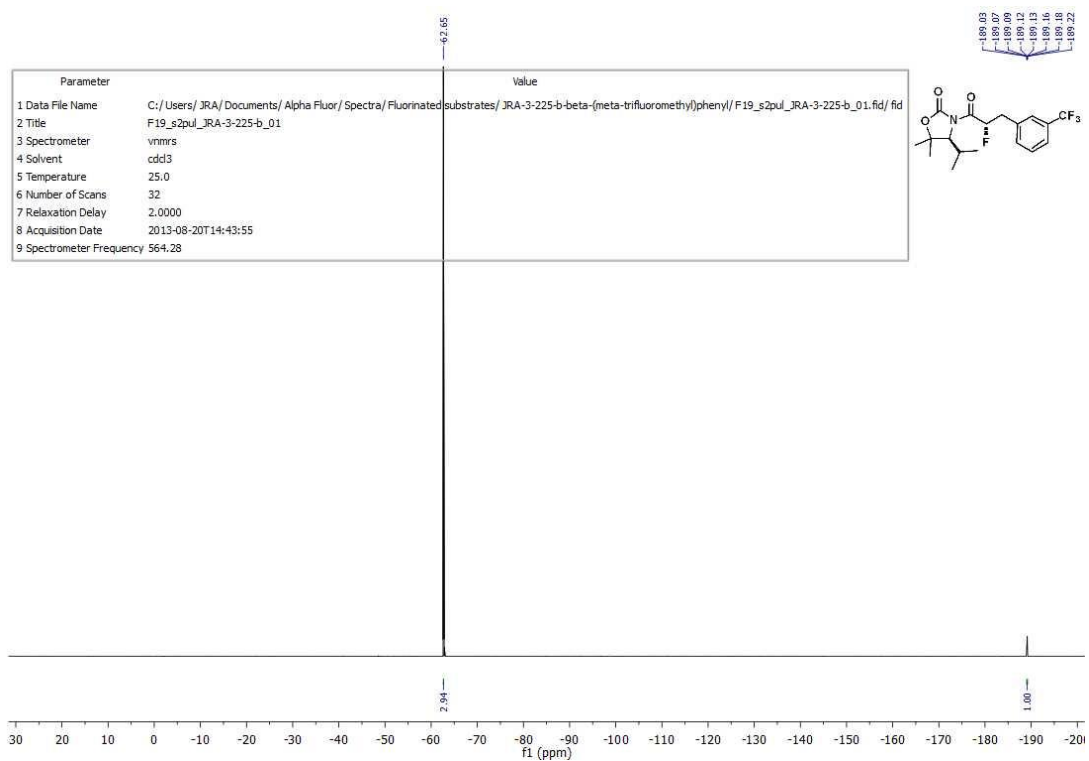


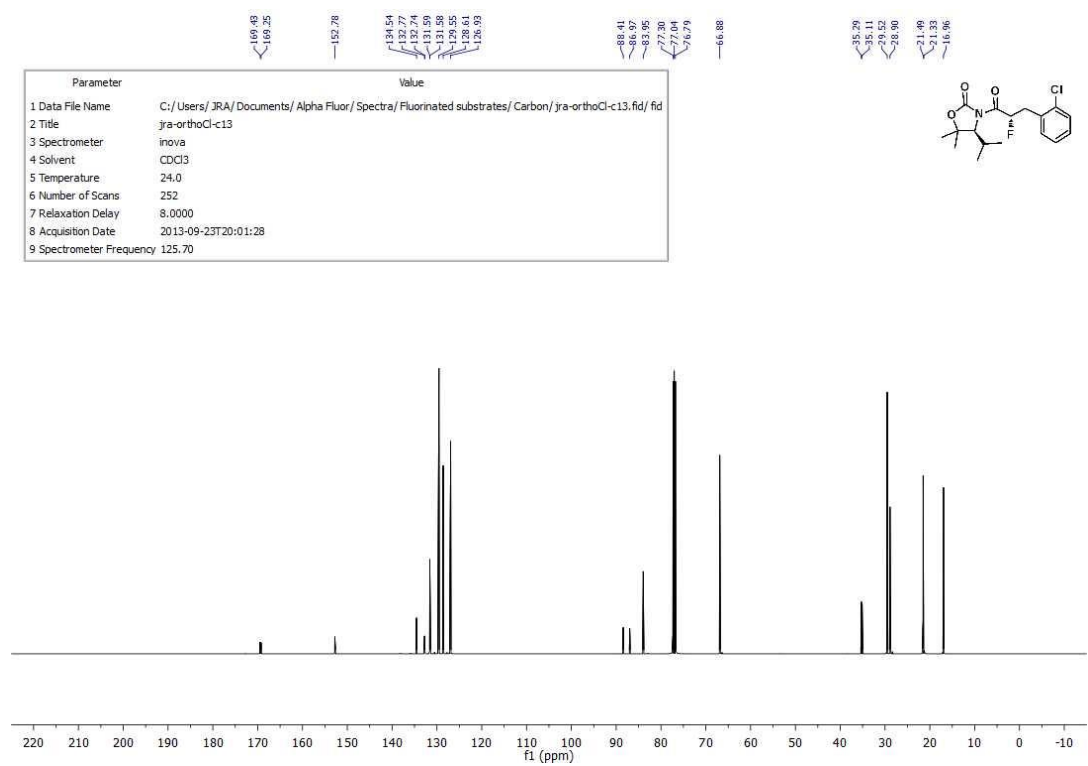
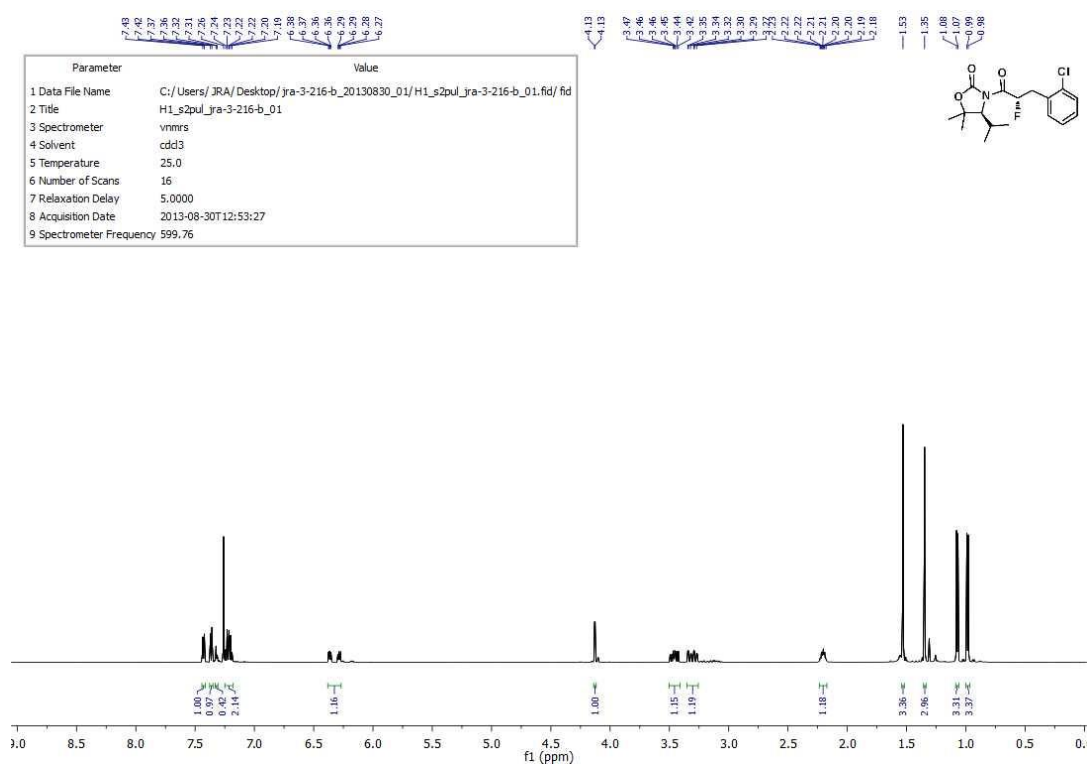


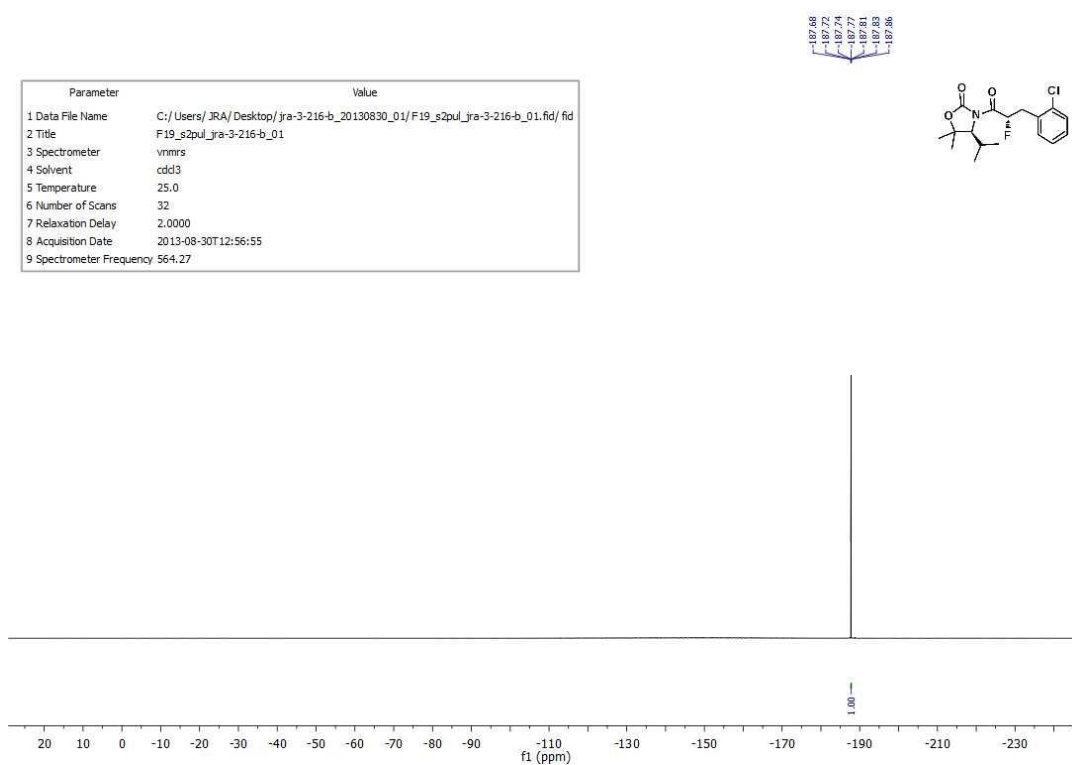


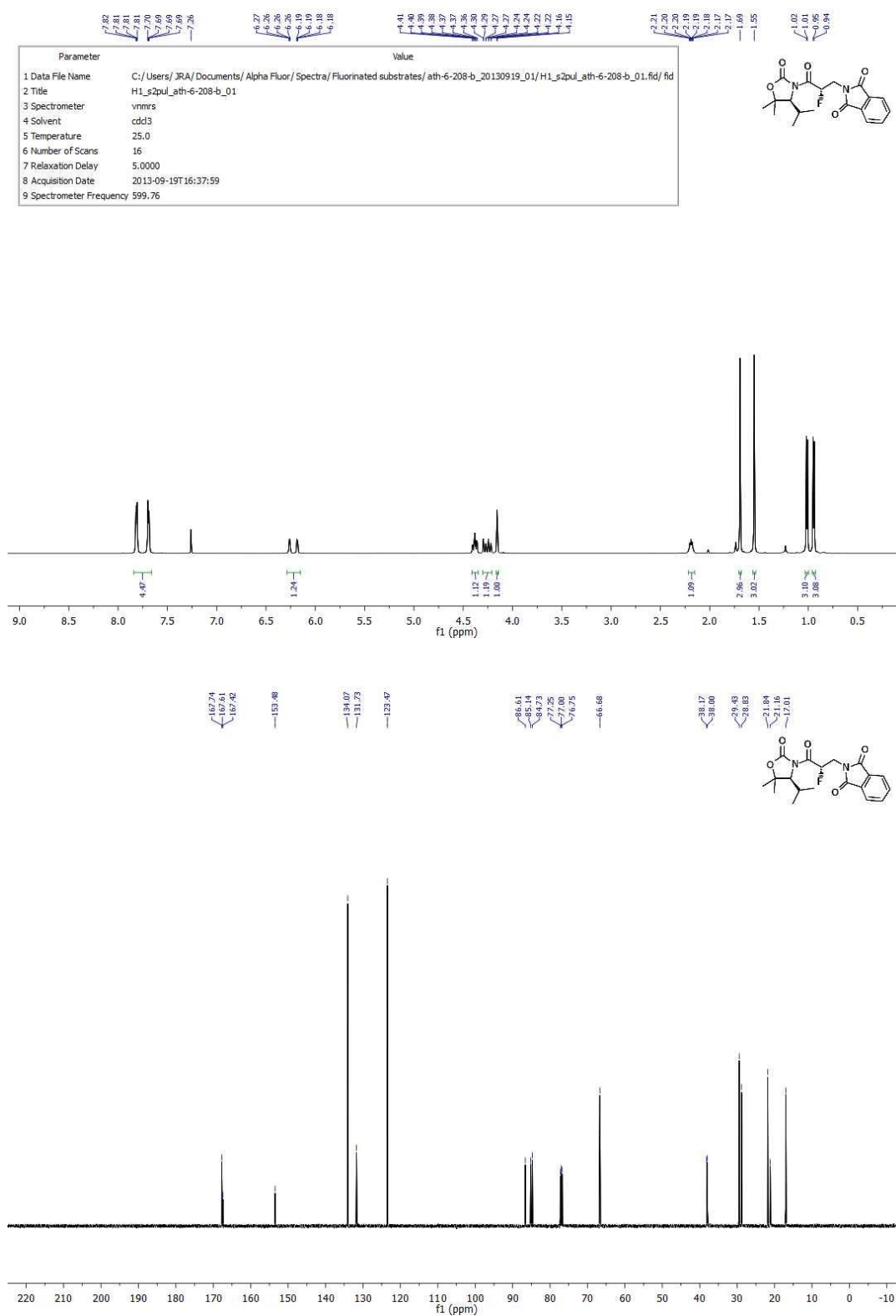


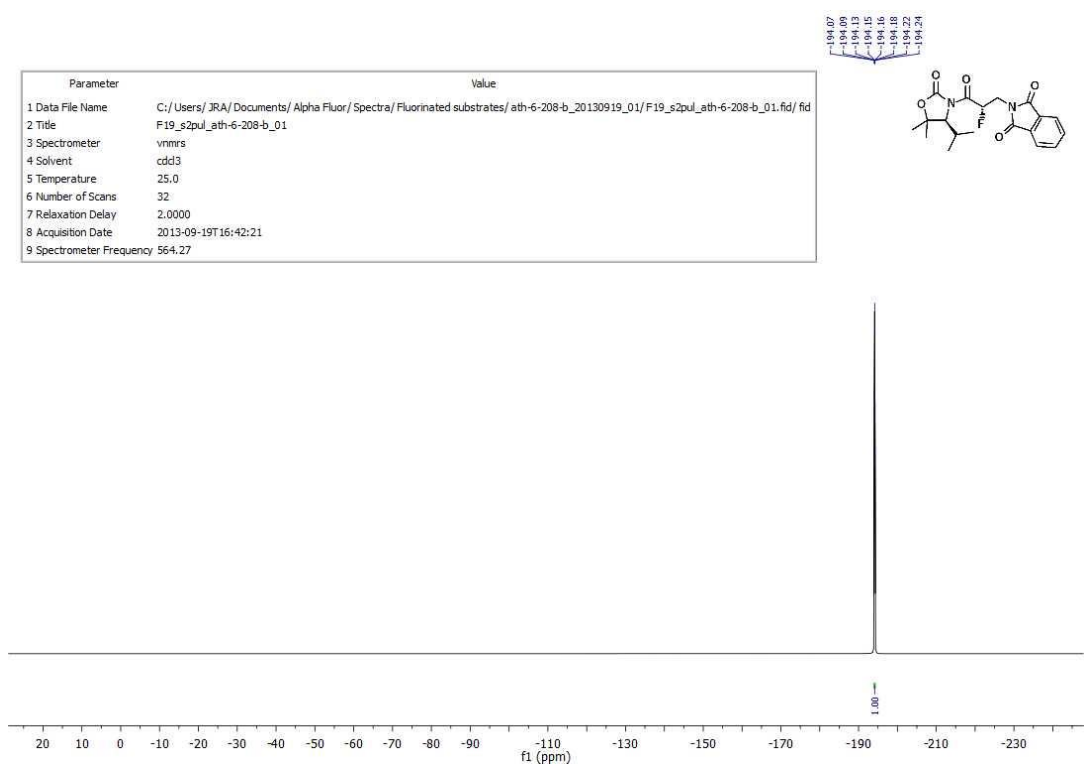


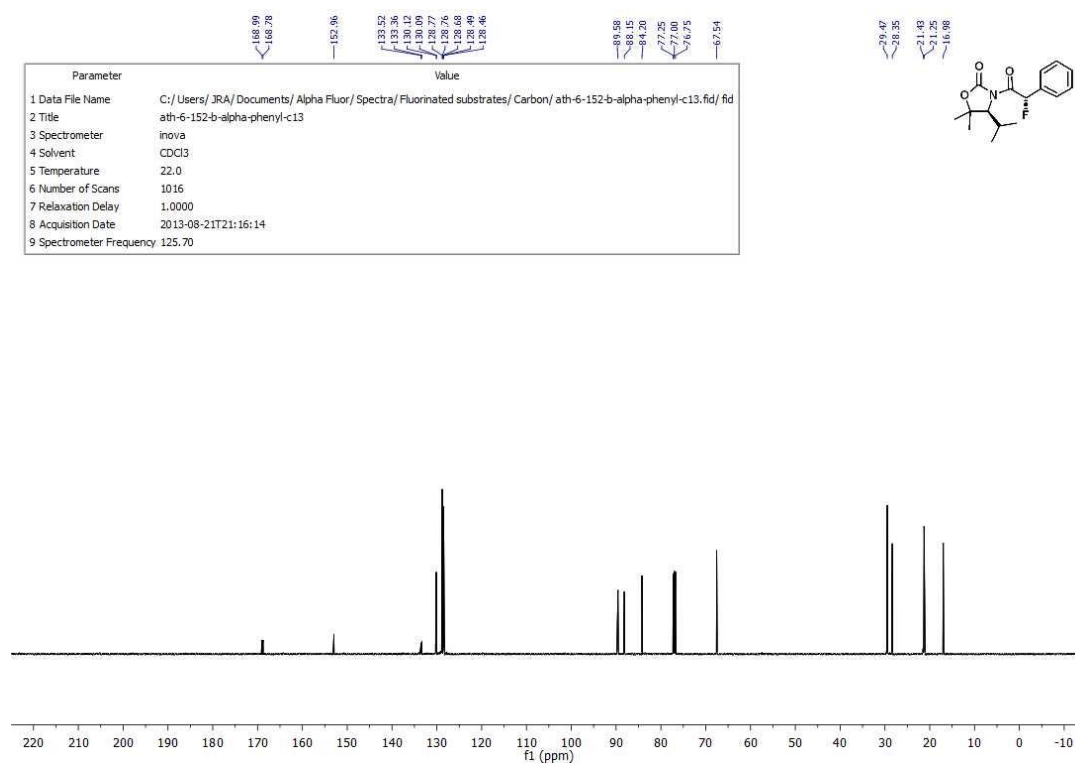
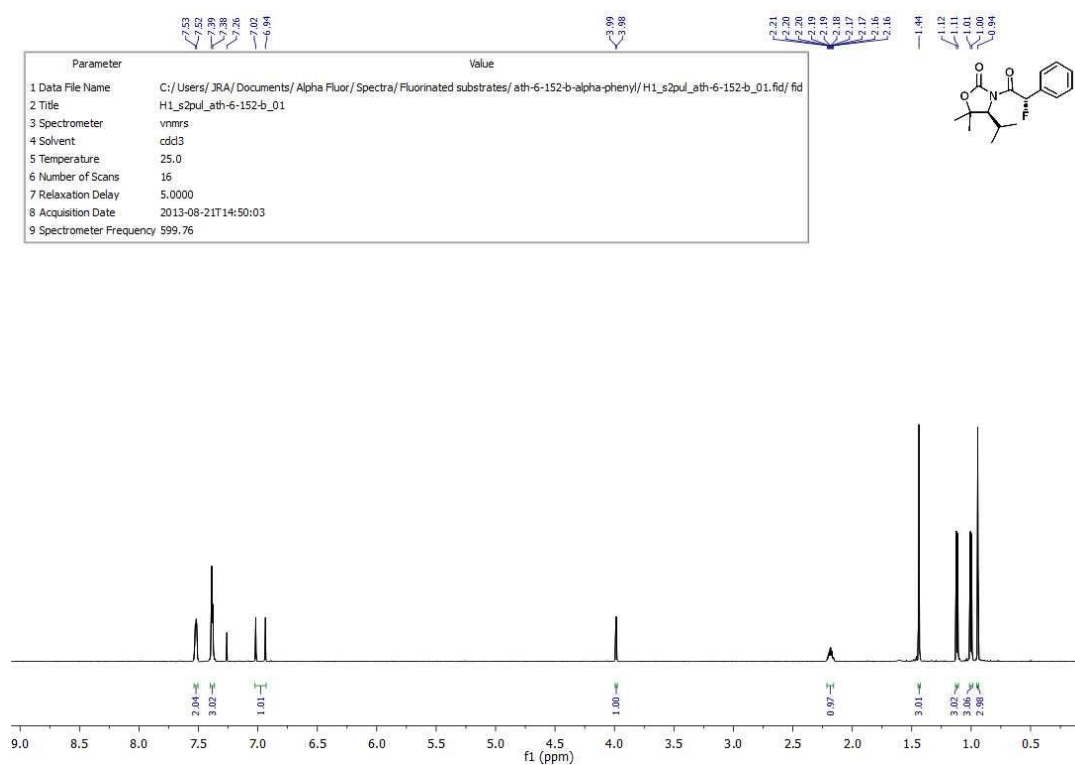




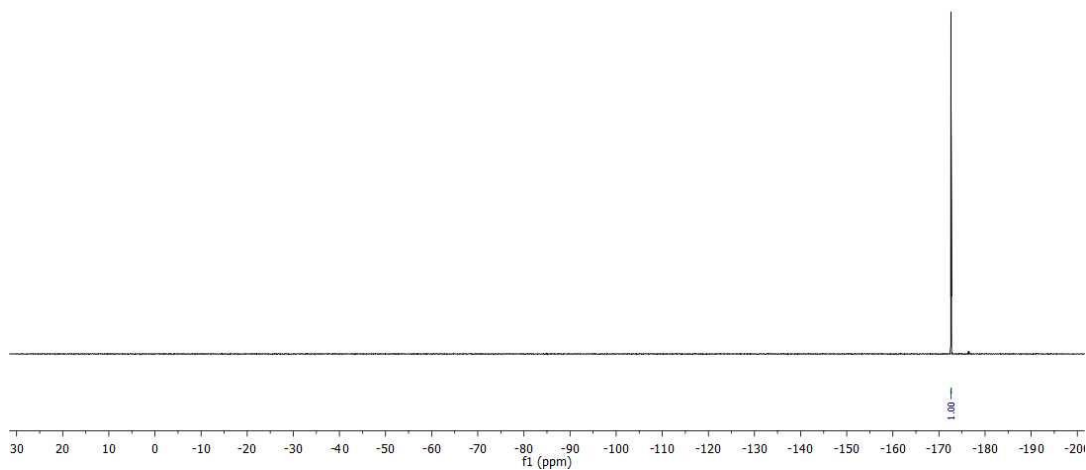
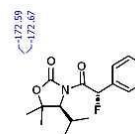


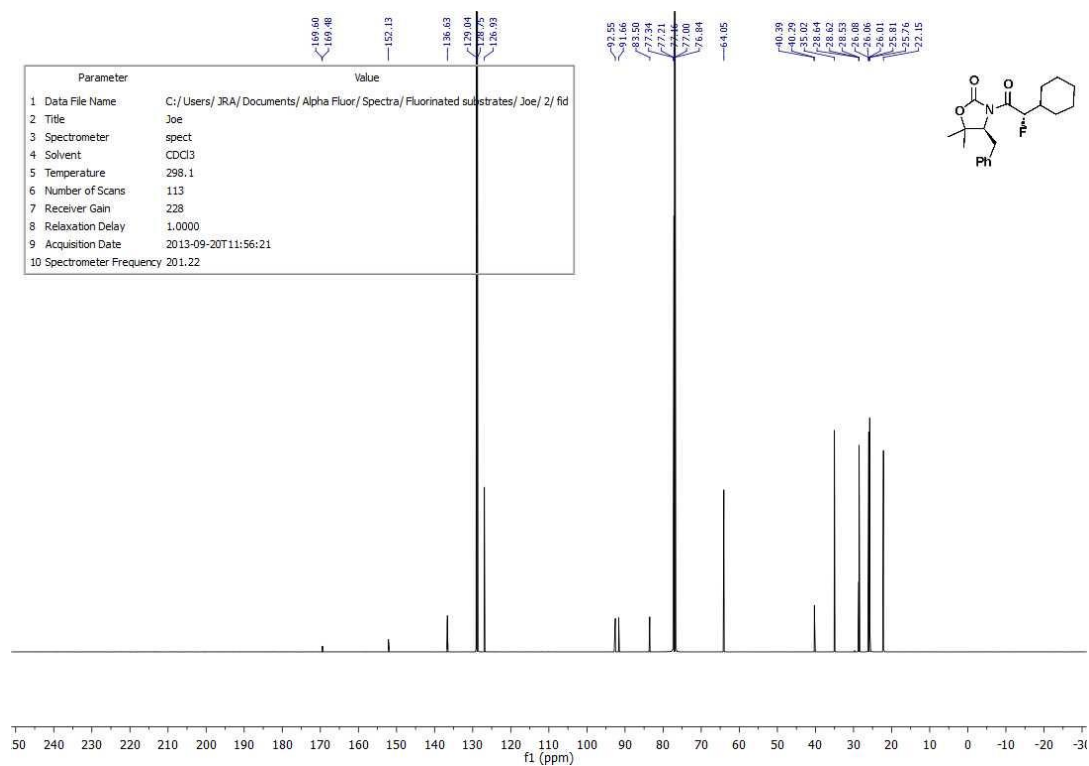
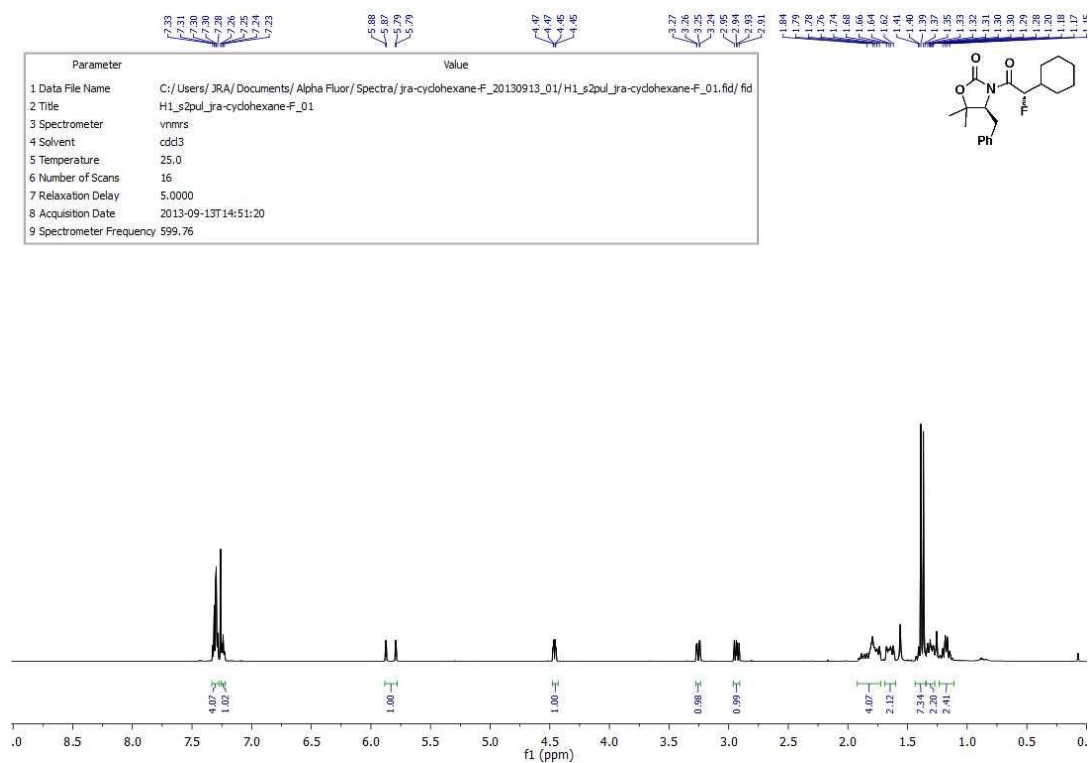


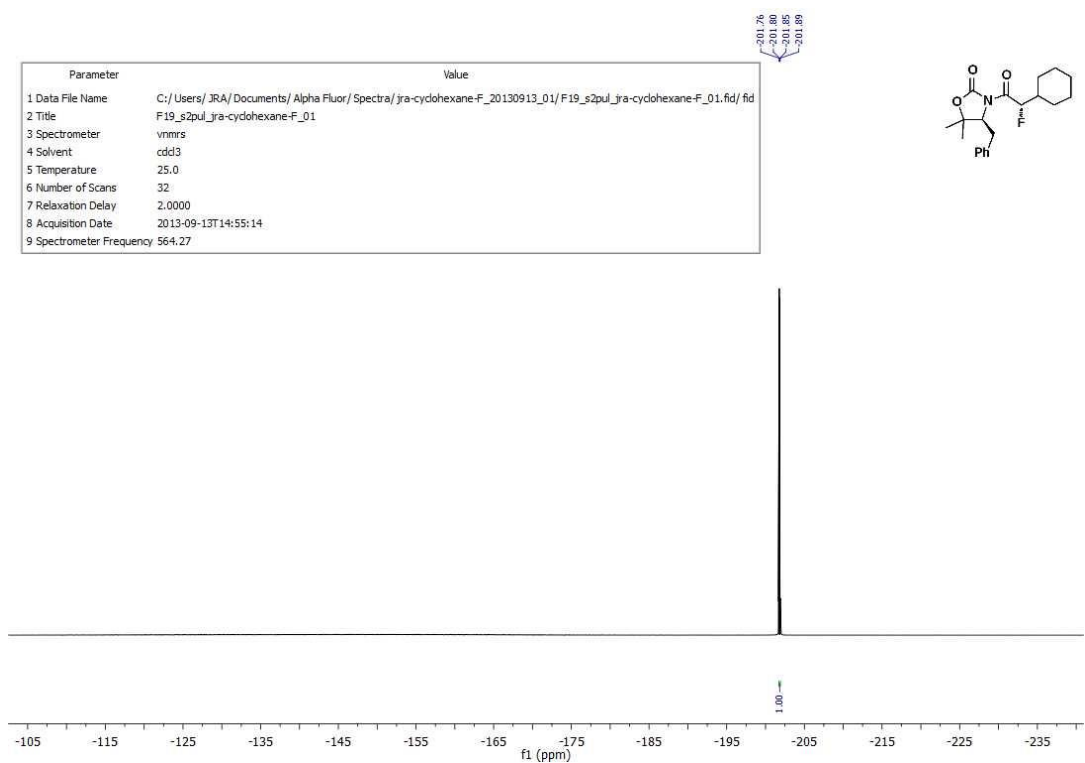


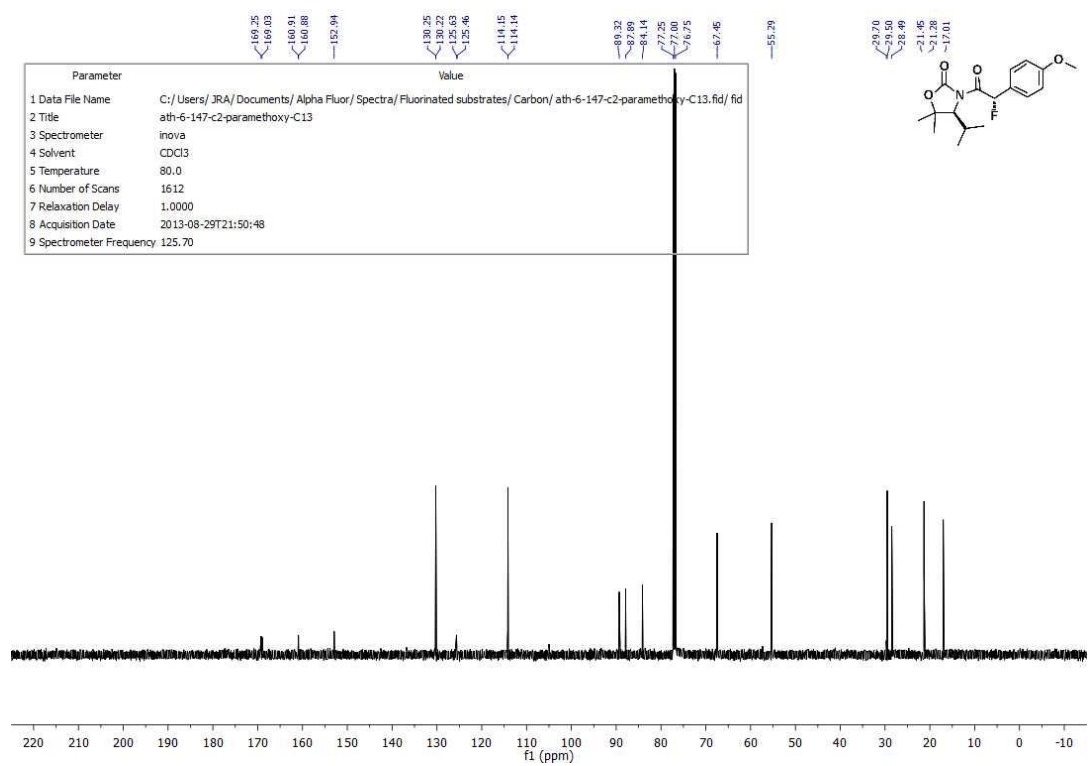
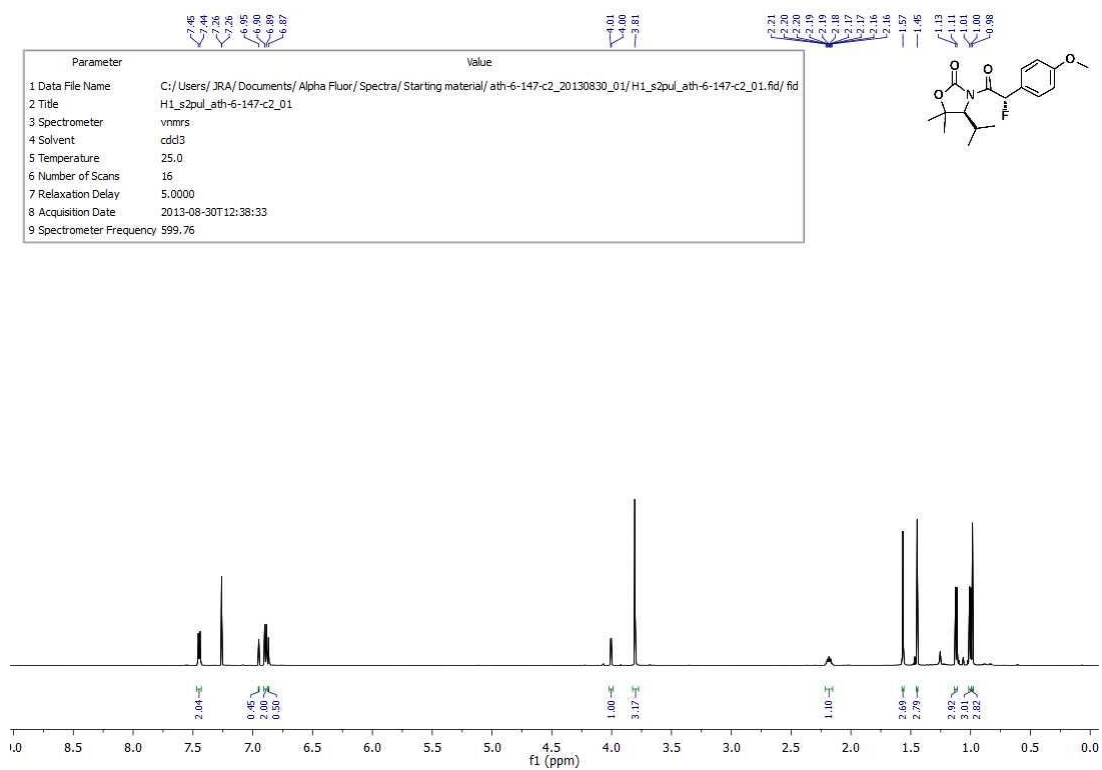


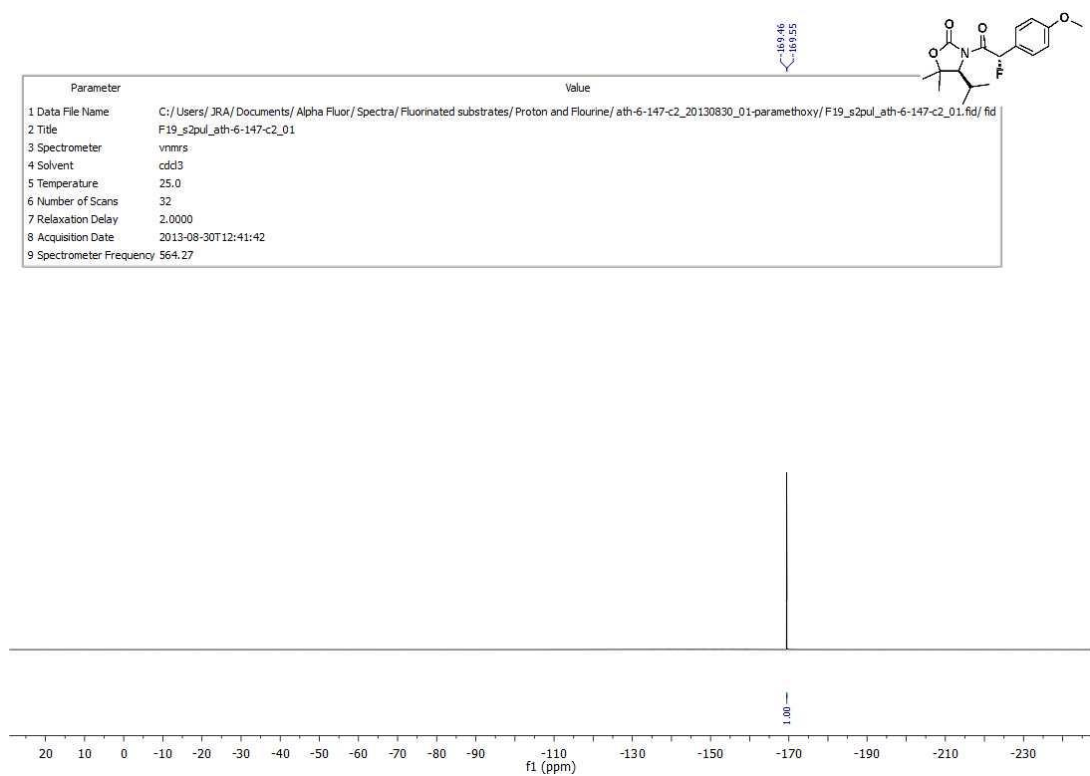
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1 Data File Name	C:/Users/JRA/Documents/Alpha Fluor/Spectra/Fluorinated substrates/ath-6-152-b-alpha-phenyl/F19_s2pul_ath-6-152-b_01.fid/fid
2 Title	F19_s2pul_ath-6-152-b_01
3 Spectrometer	nmrns
4 Solvent	cdcl3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-08-21T14:53:39
9 Spectrometer Frequency	564.28

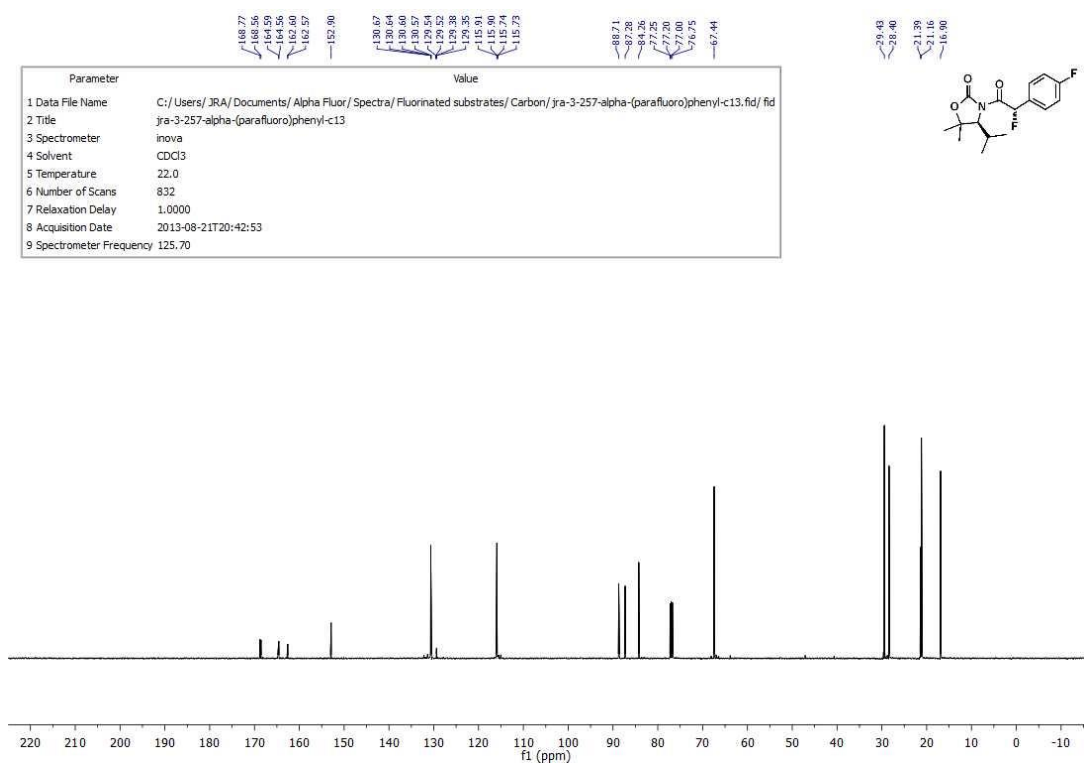
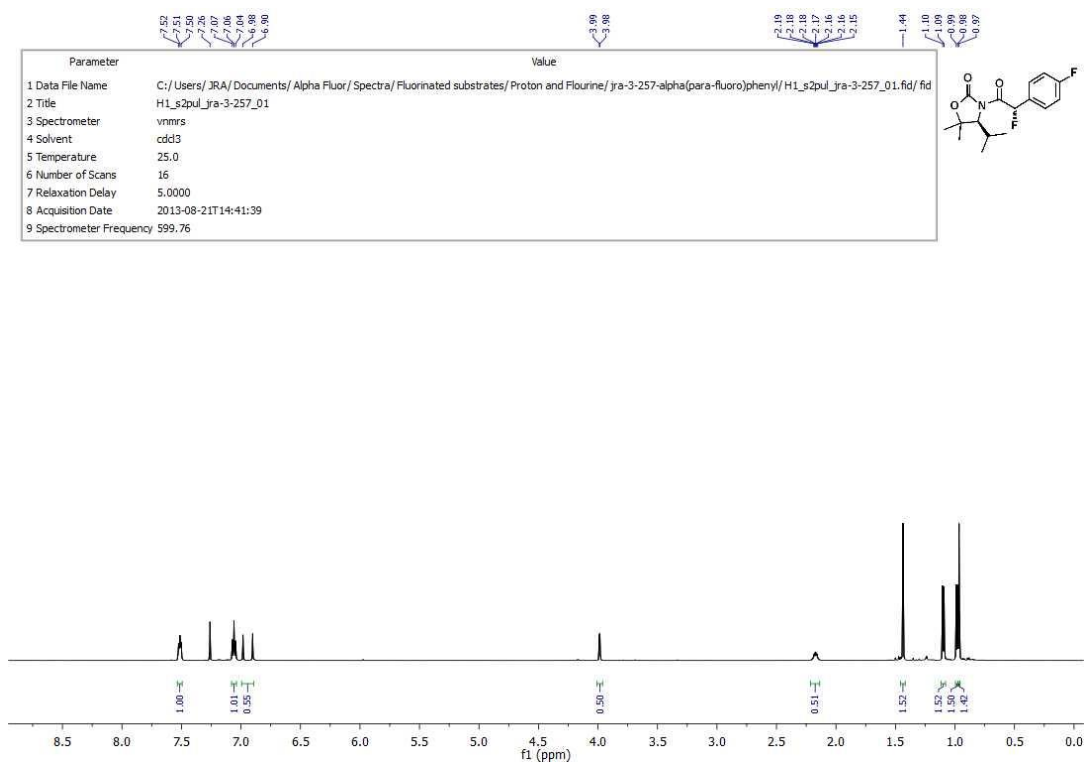


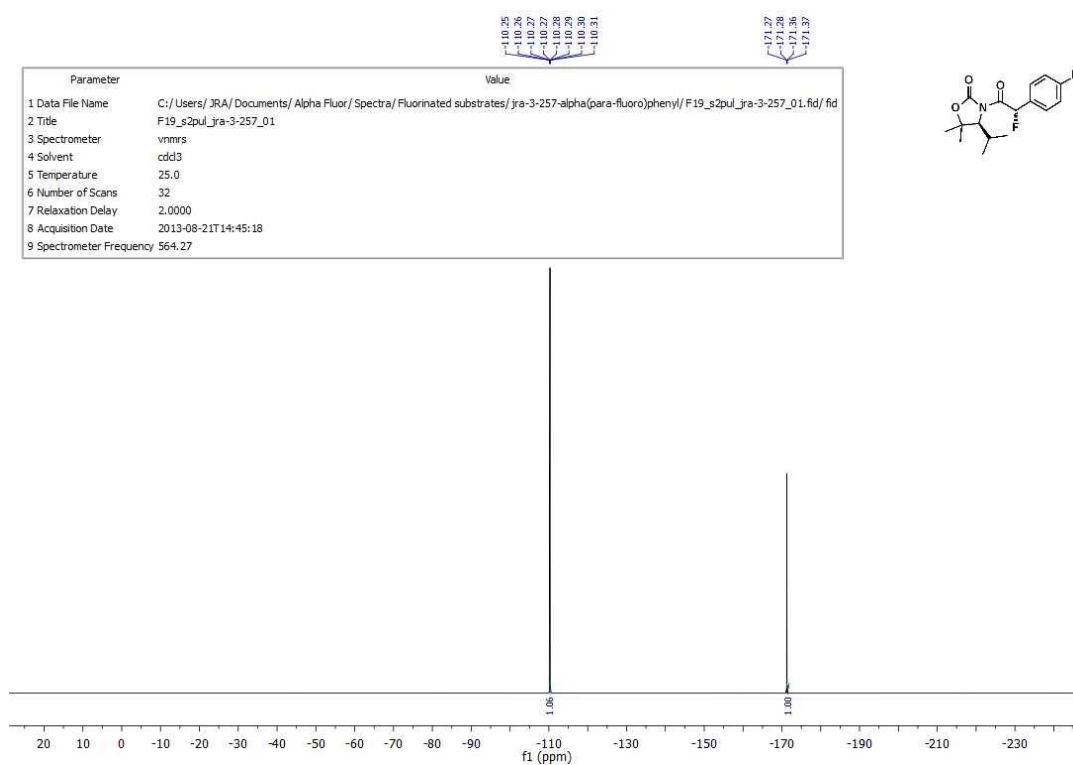


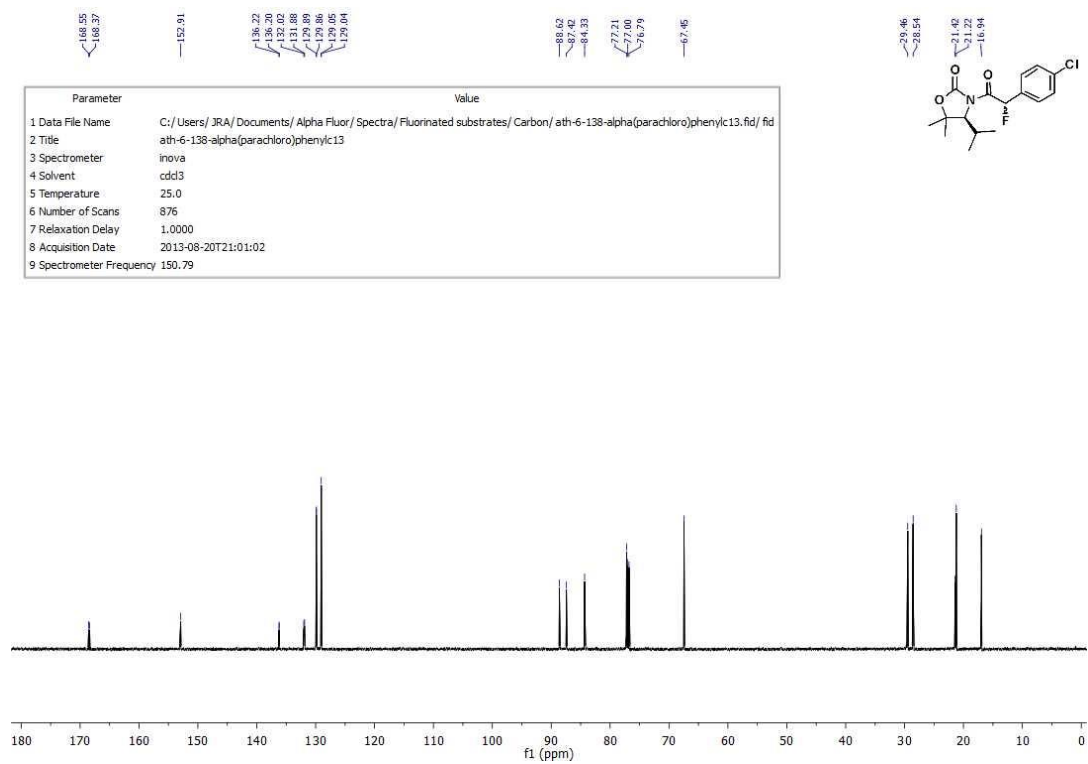
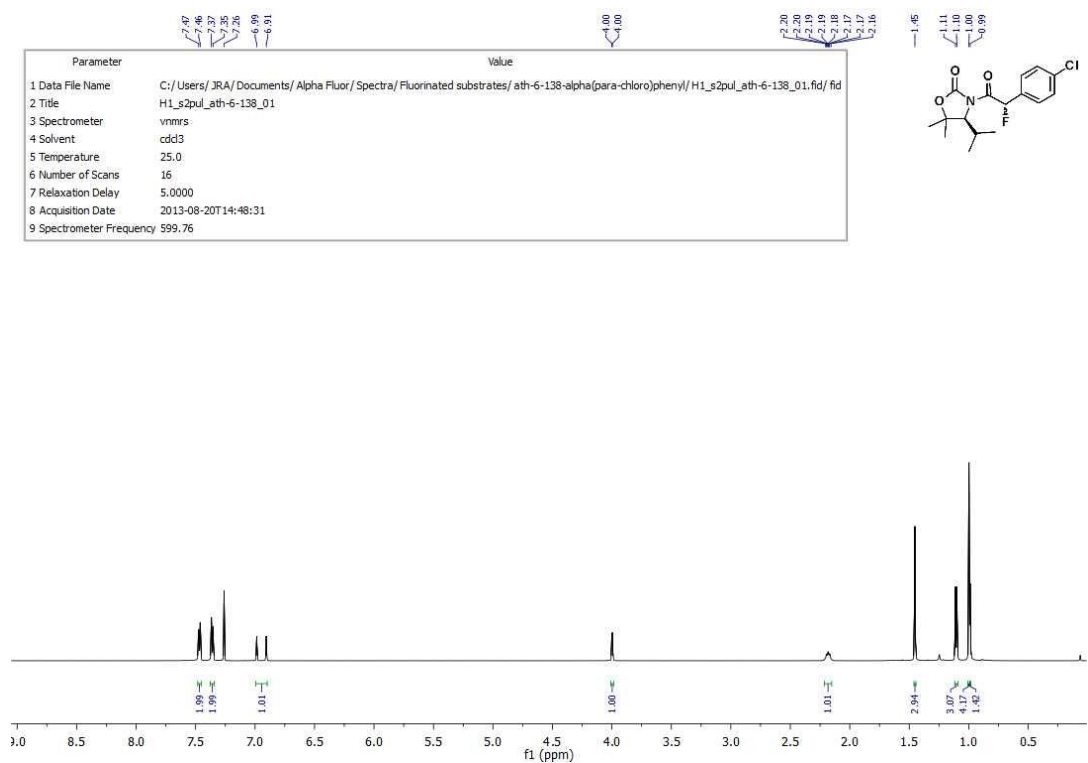




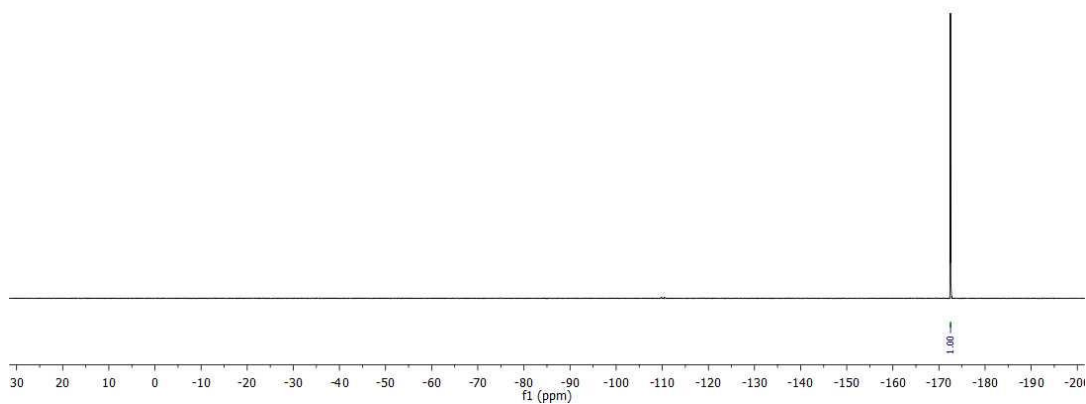
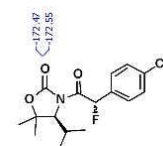


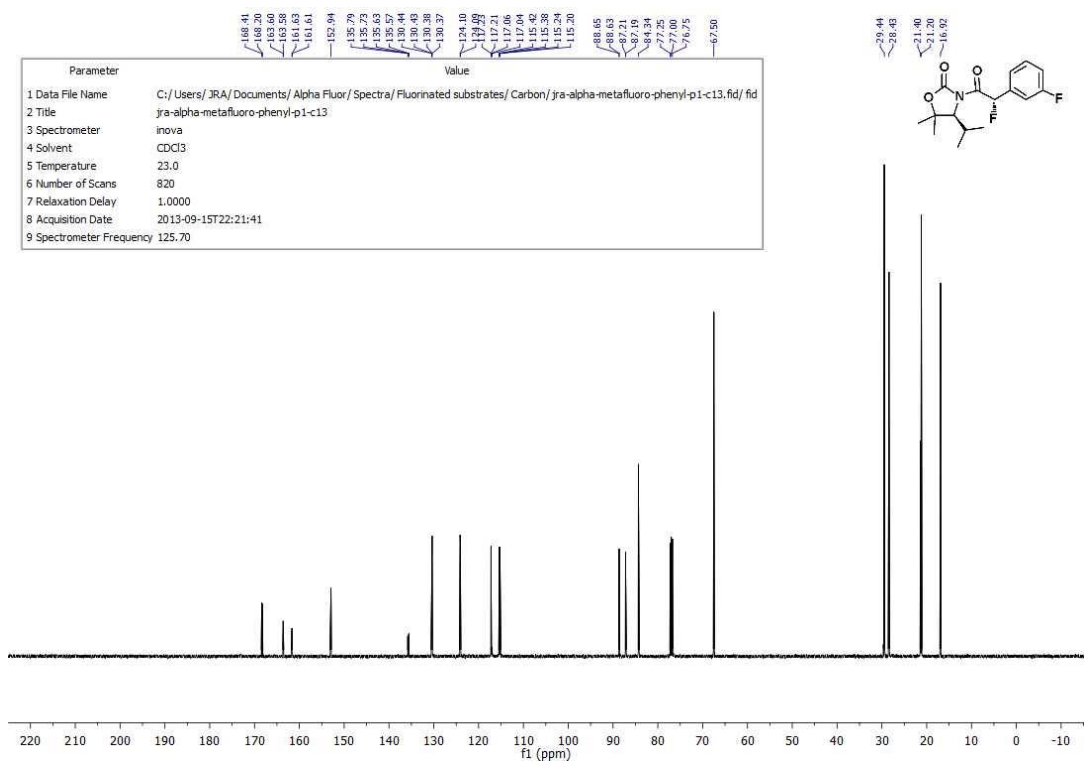
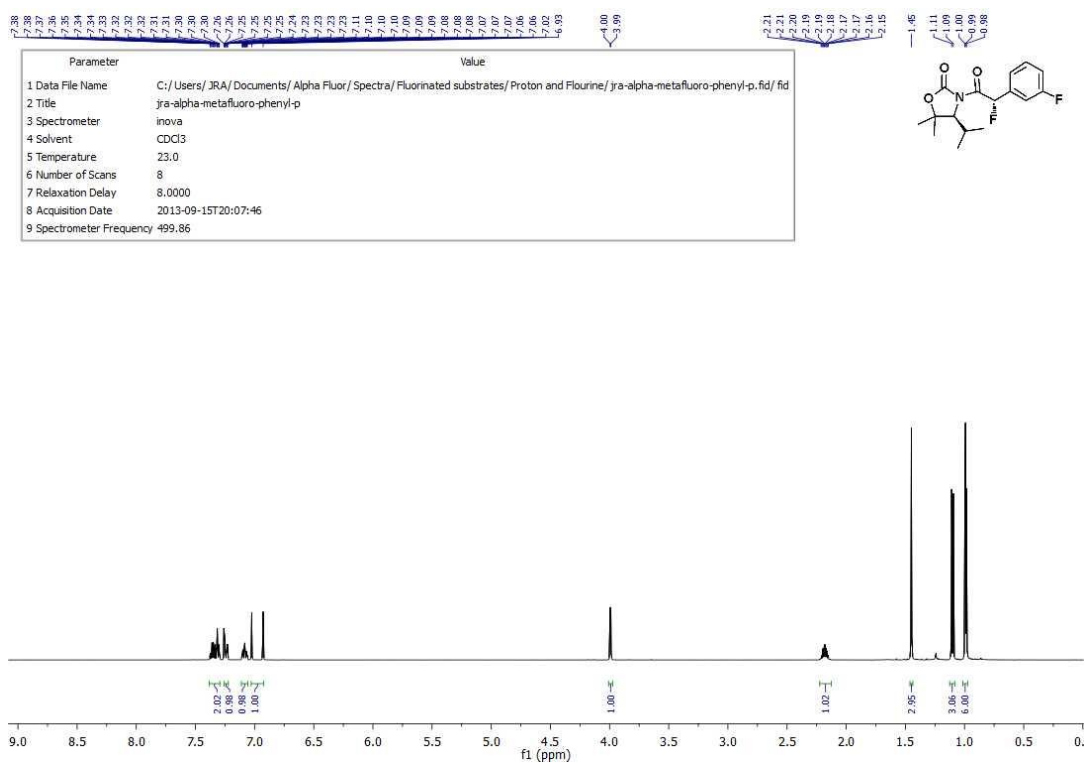


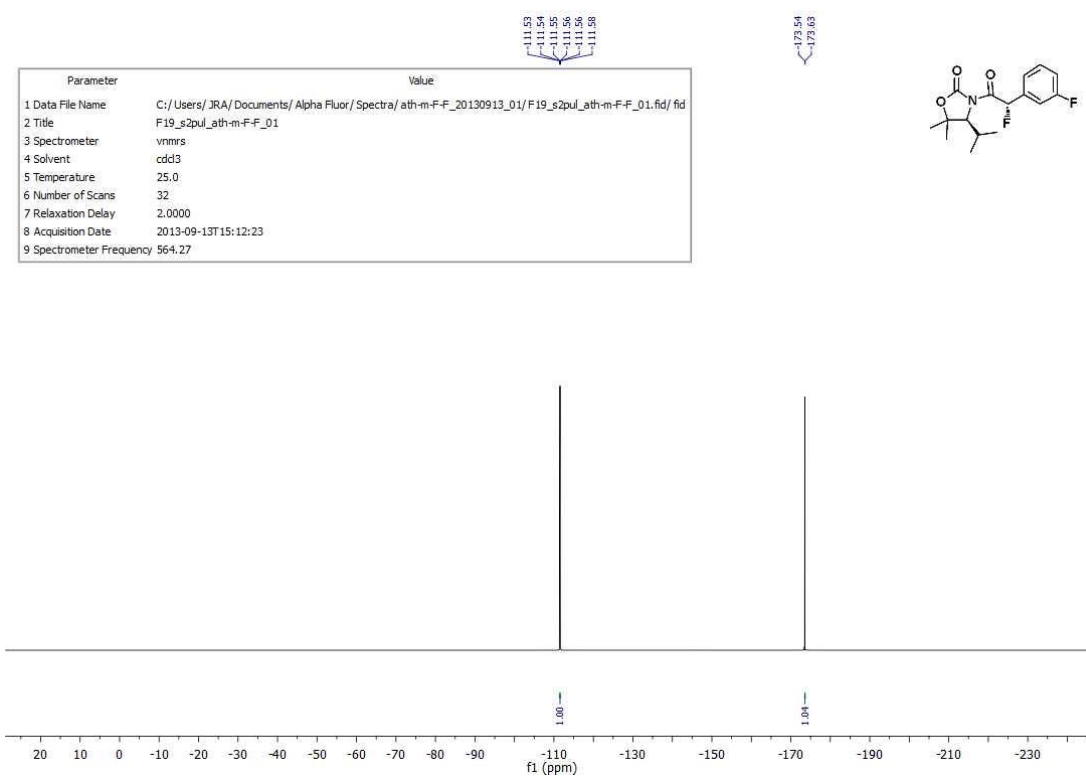


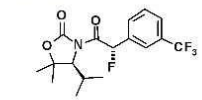
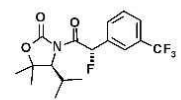


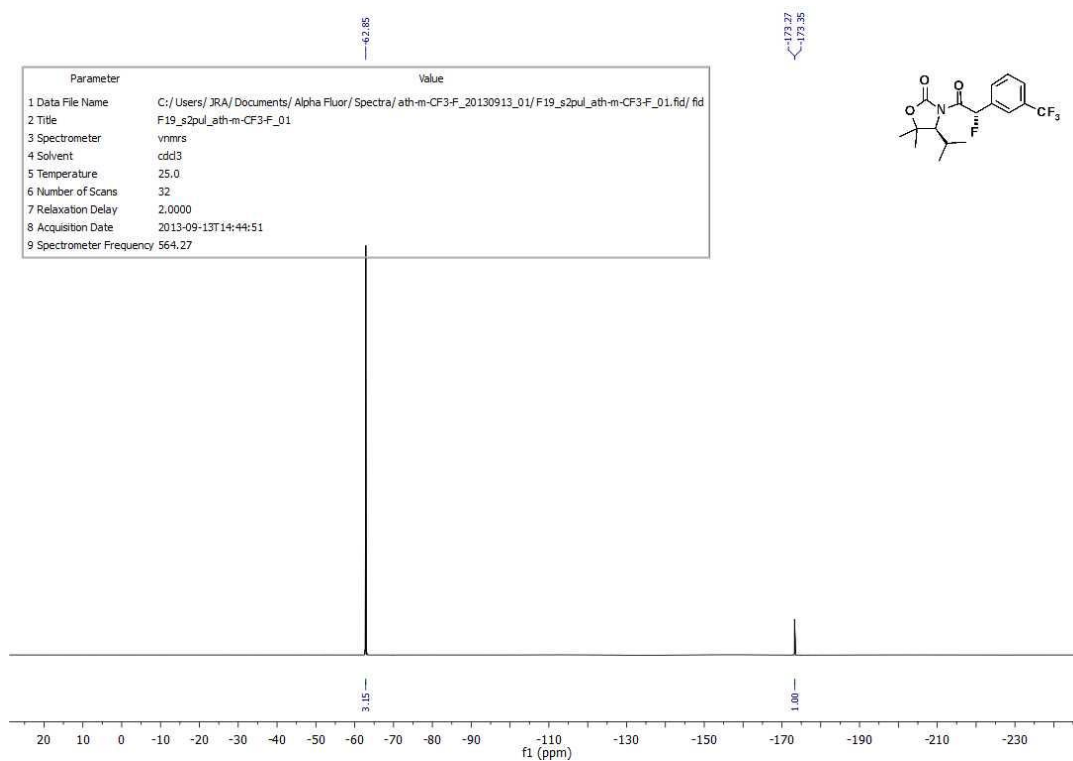
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1 Data File Name	C:/Users/JRA/Documents/Alpha Fluor/Spectra/Fluorinated substrates/ath-6-138-alpha(para-chloro)phenyl/F19_s2pul_ath-6-138_01.fid
2 Title	F19_s2pul_ath-6-138_01
3 Spectrometer	nmrns
4 Solvent	cdcl3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-08-20T14:51:50
9 Spectrometer Frequency	564.28

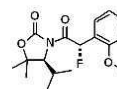
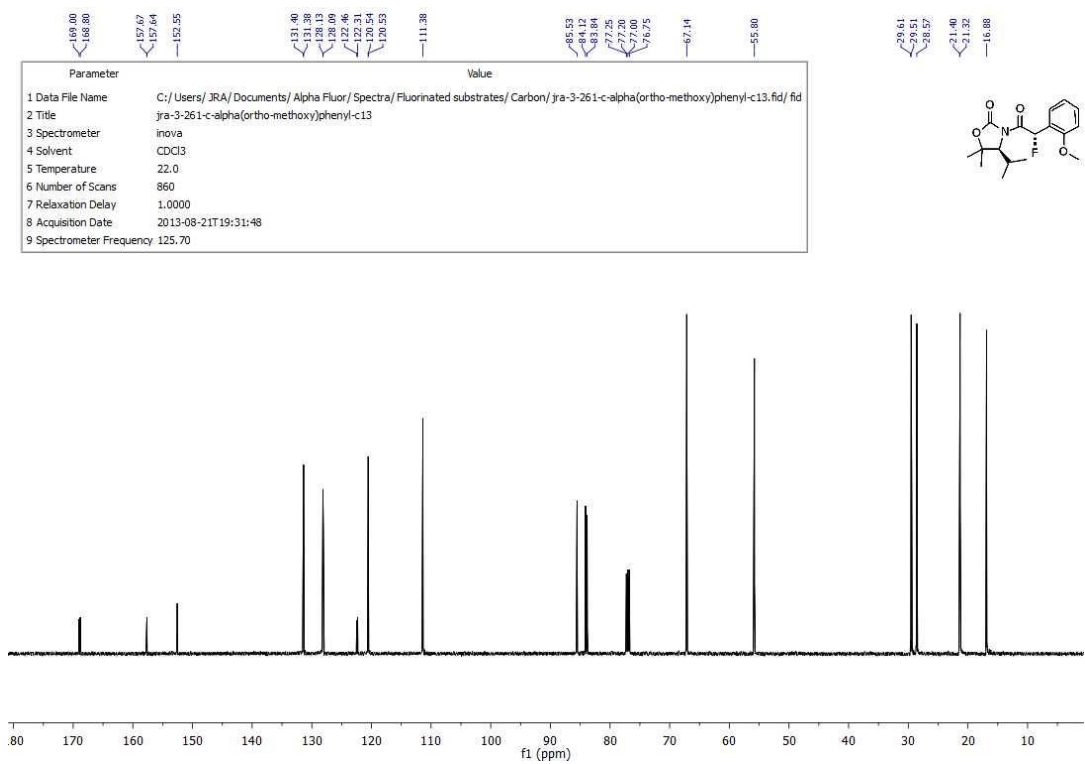
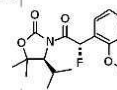
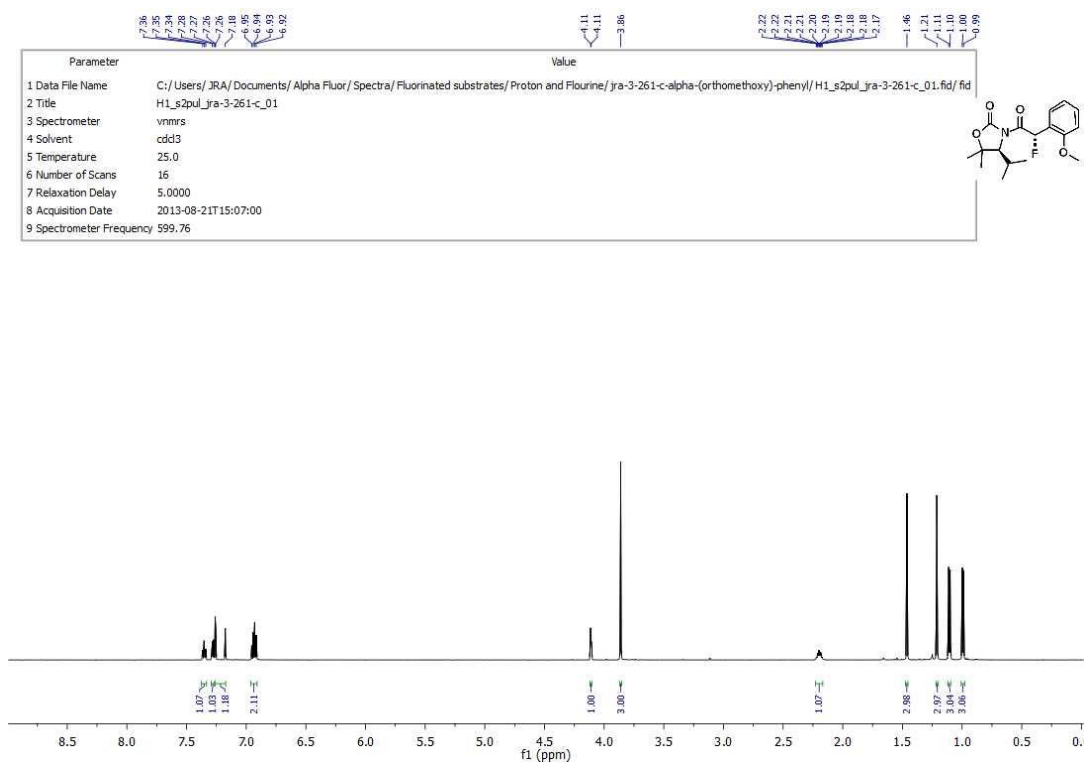


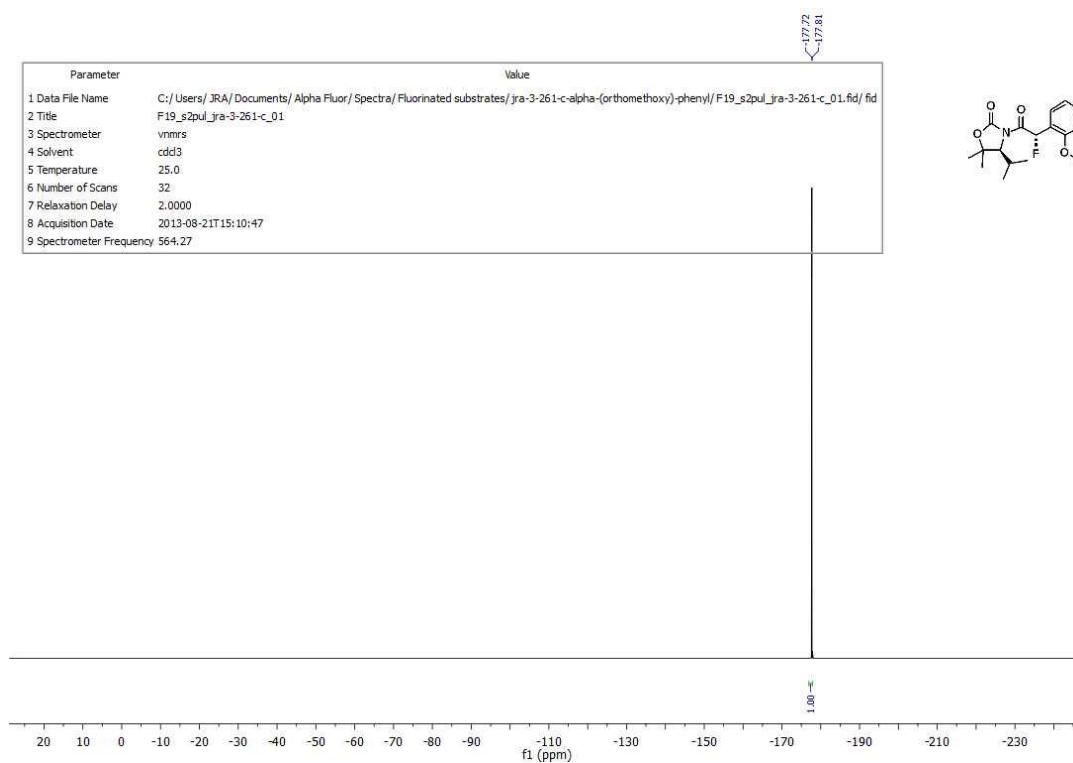


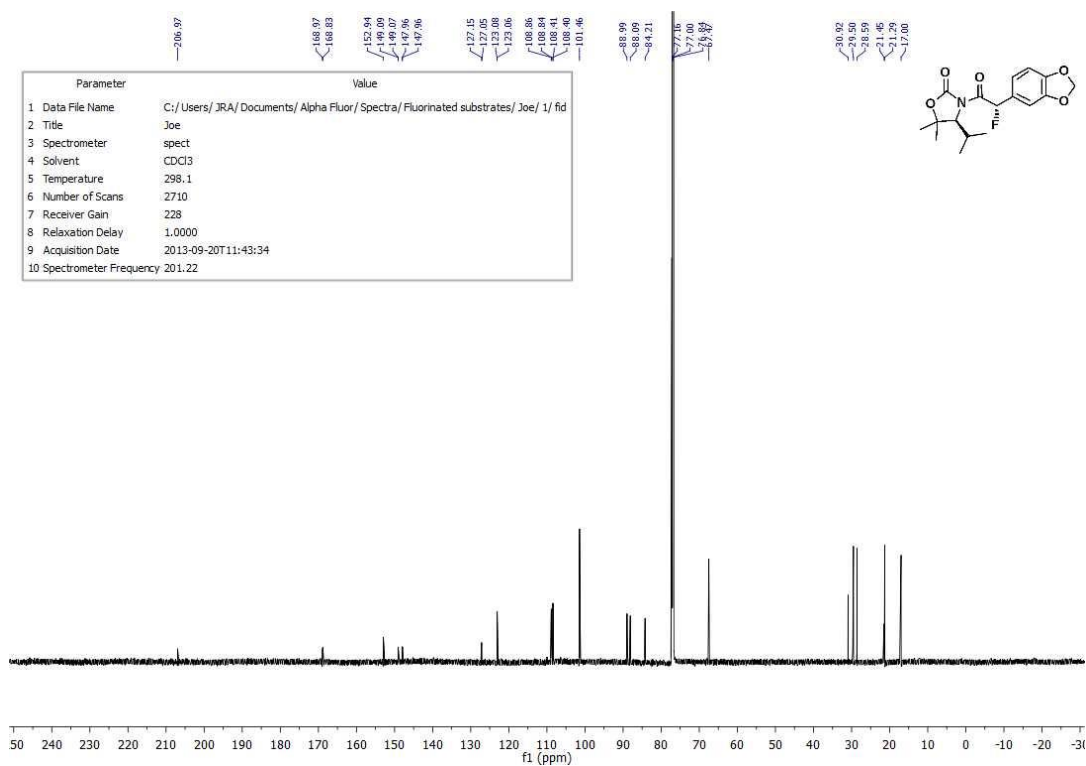
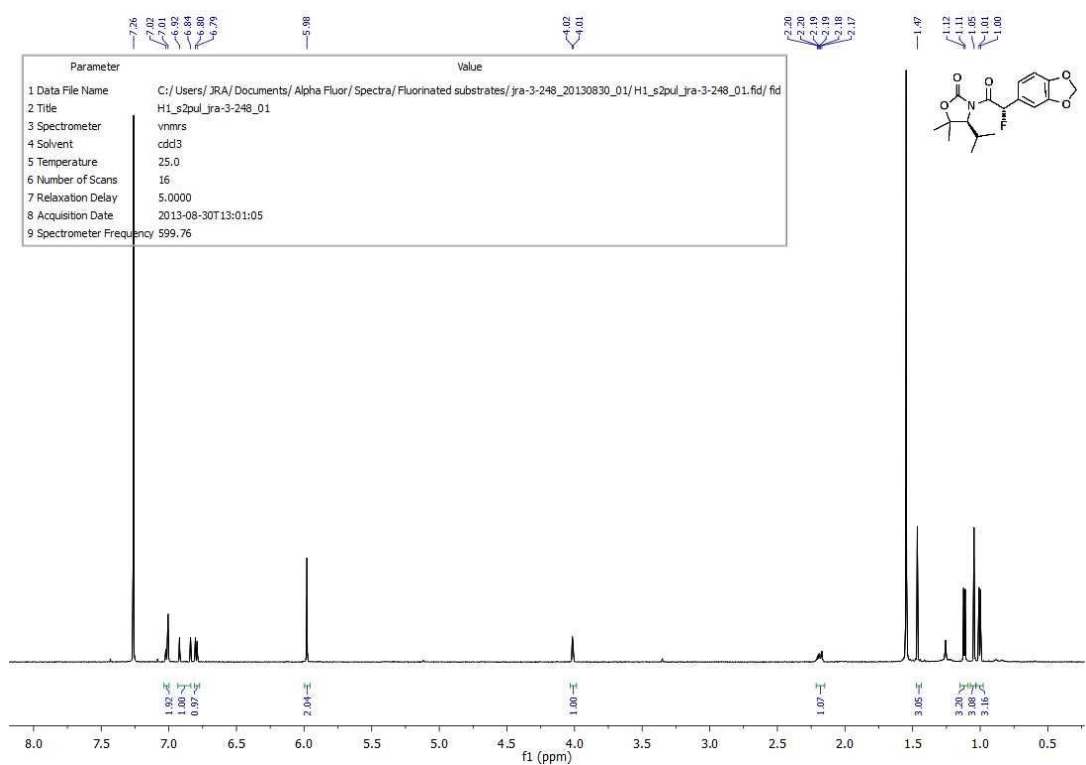




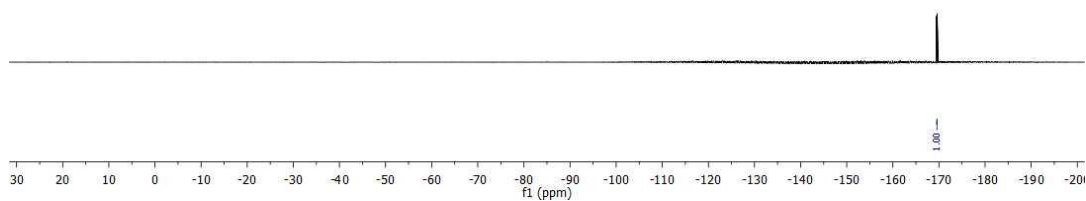
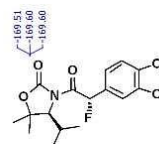


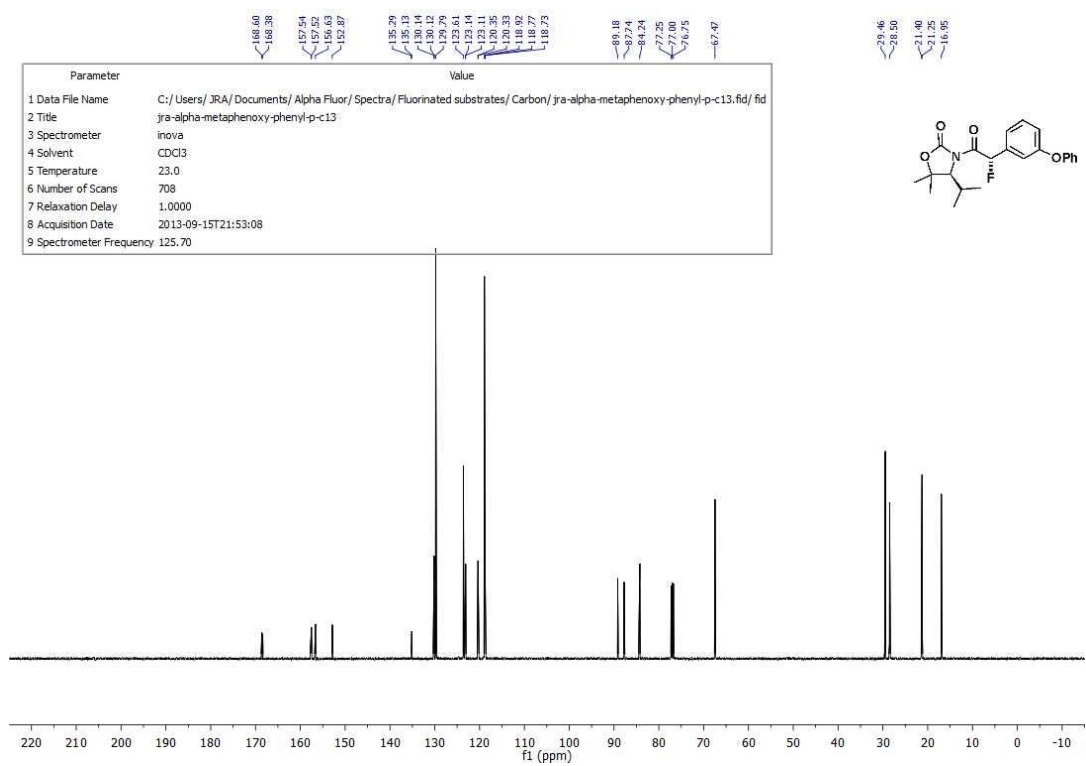
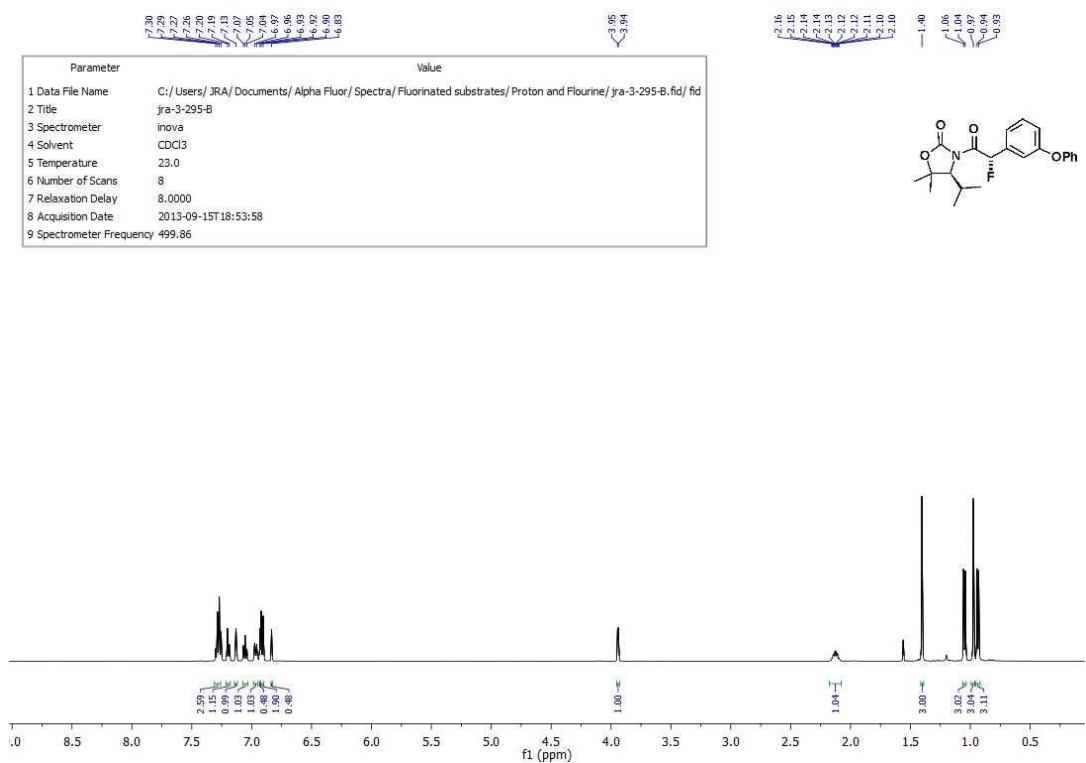


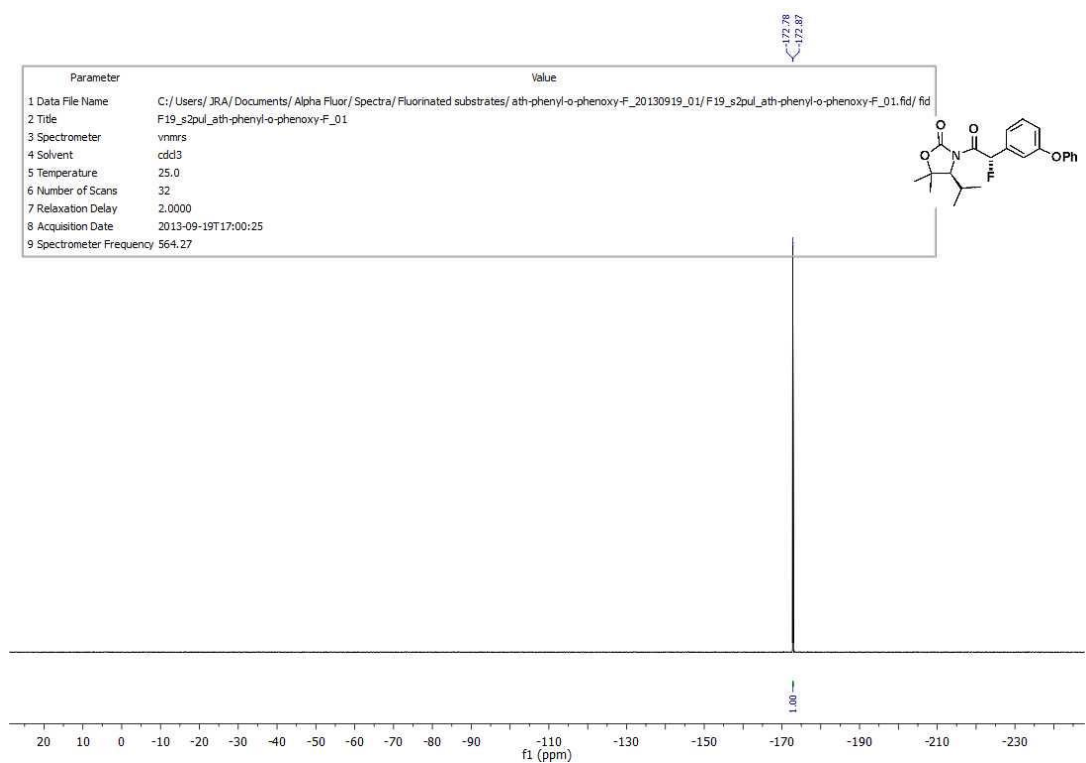


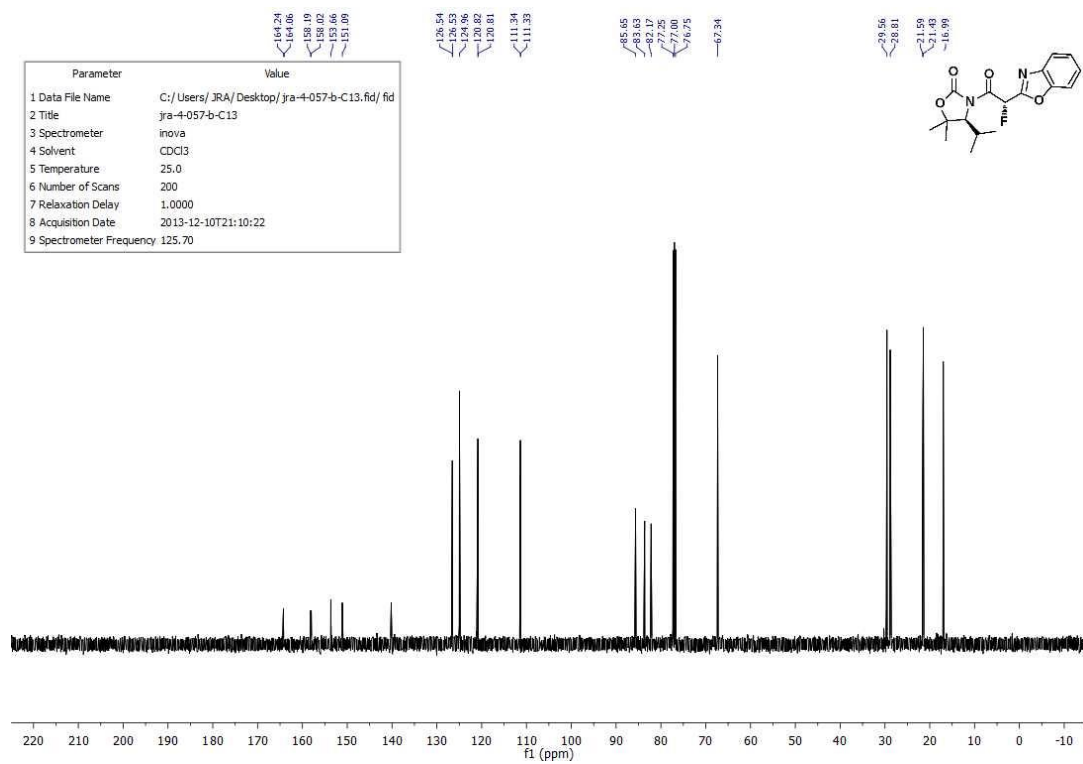
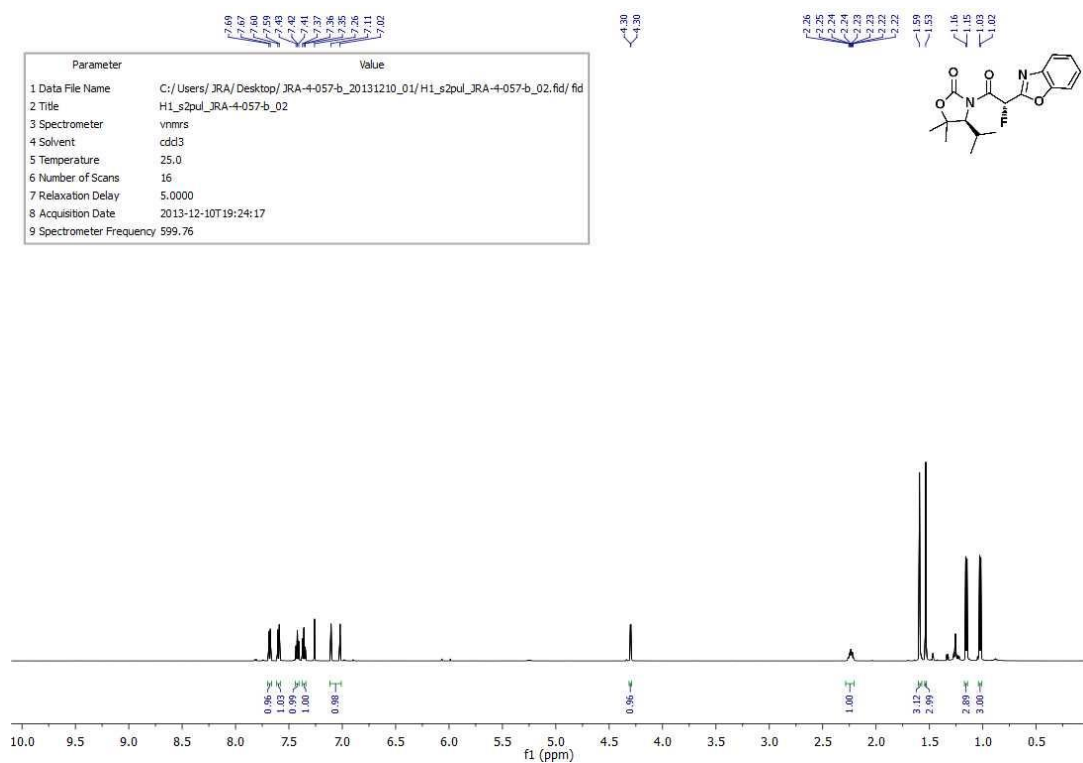


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2 Title	F19_s2pul_jra-3-248_01
3 Spectrometer	nmrns
4 Solvent	cdcl3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-08-30T13:04:33
9 Spectrometer Frequency	564.28

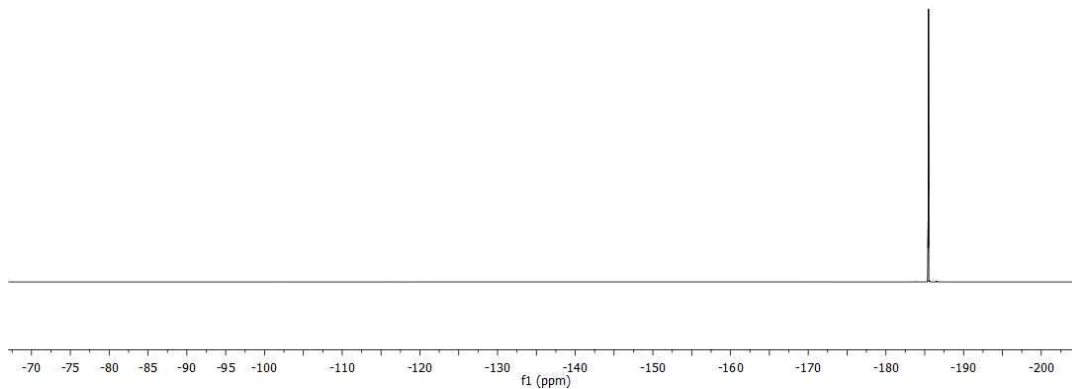
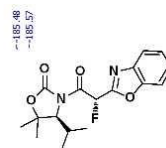


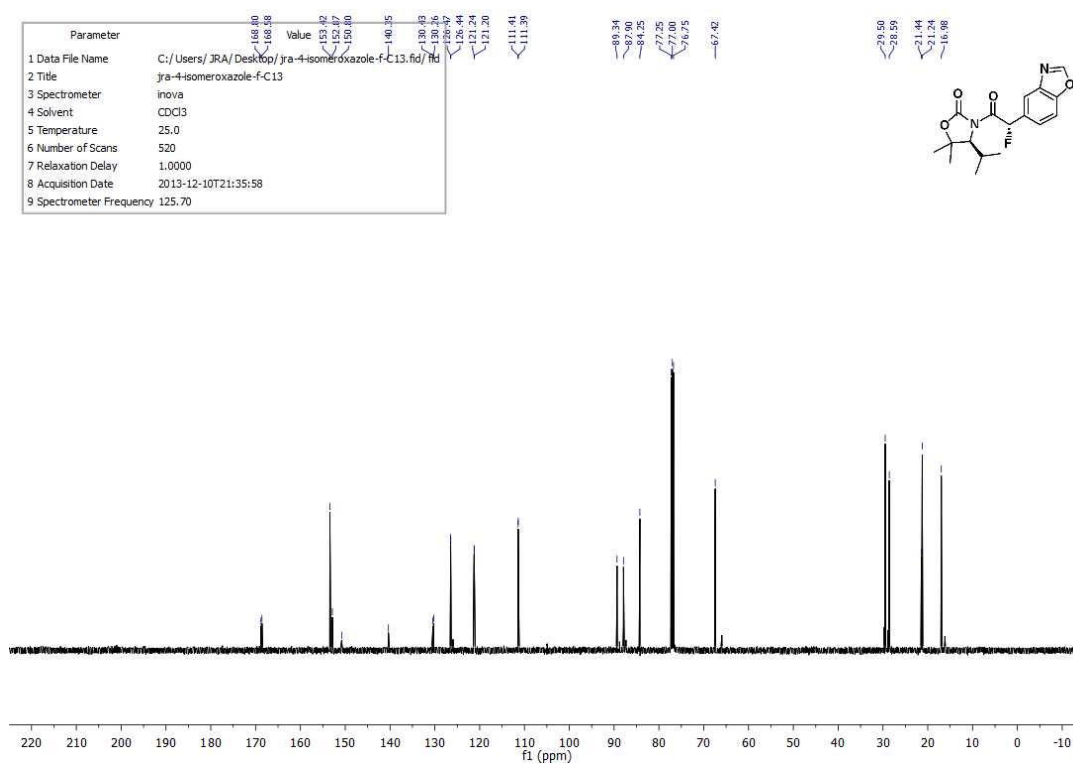
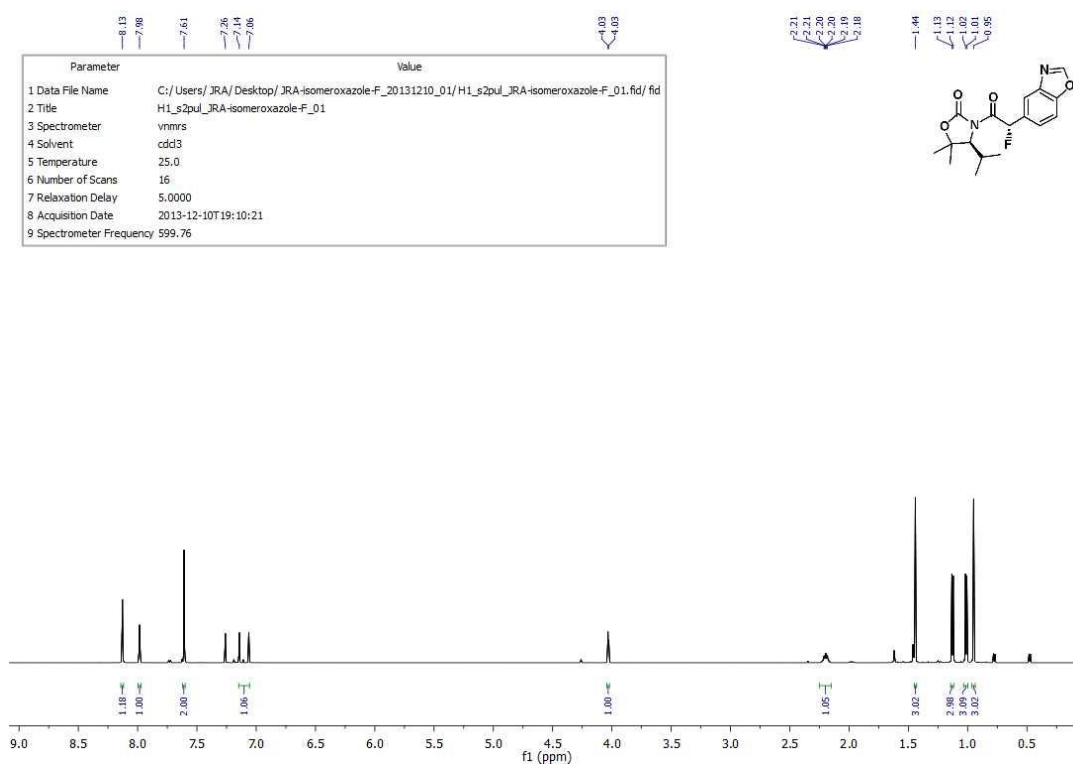


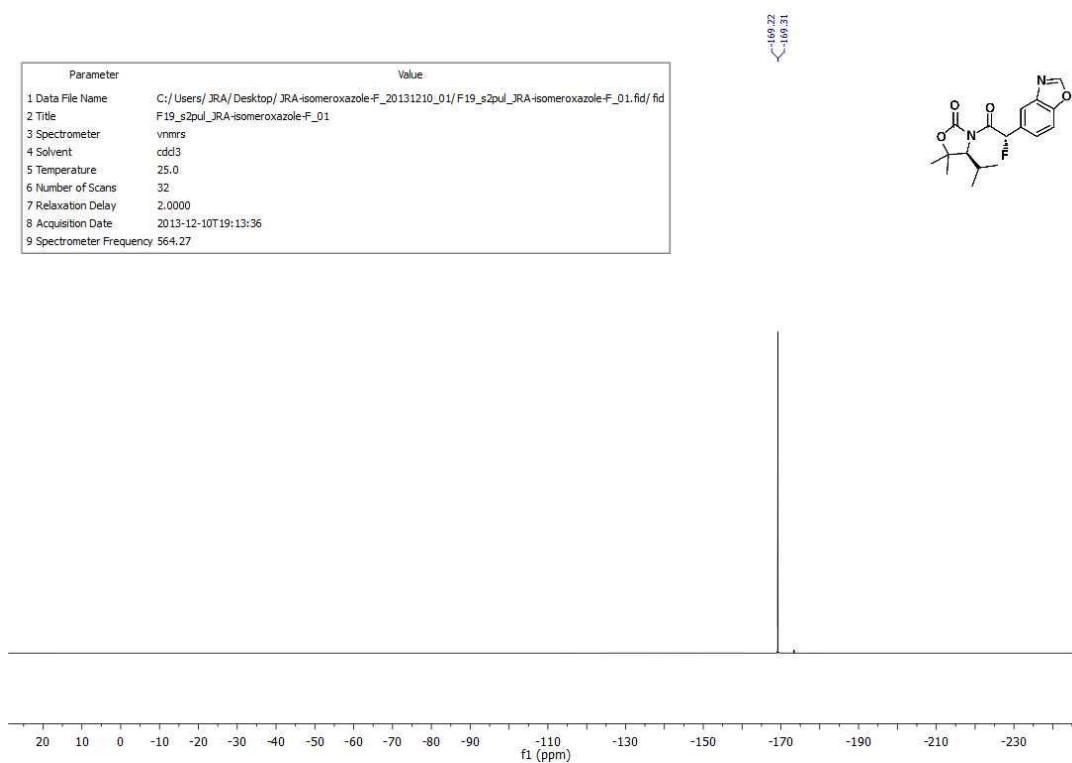


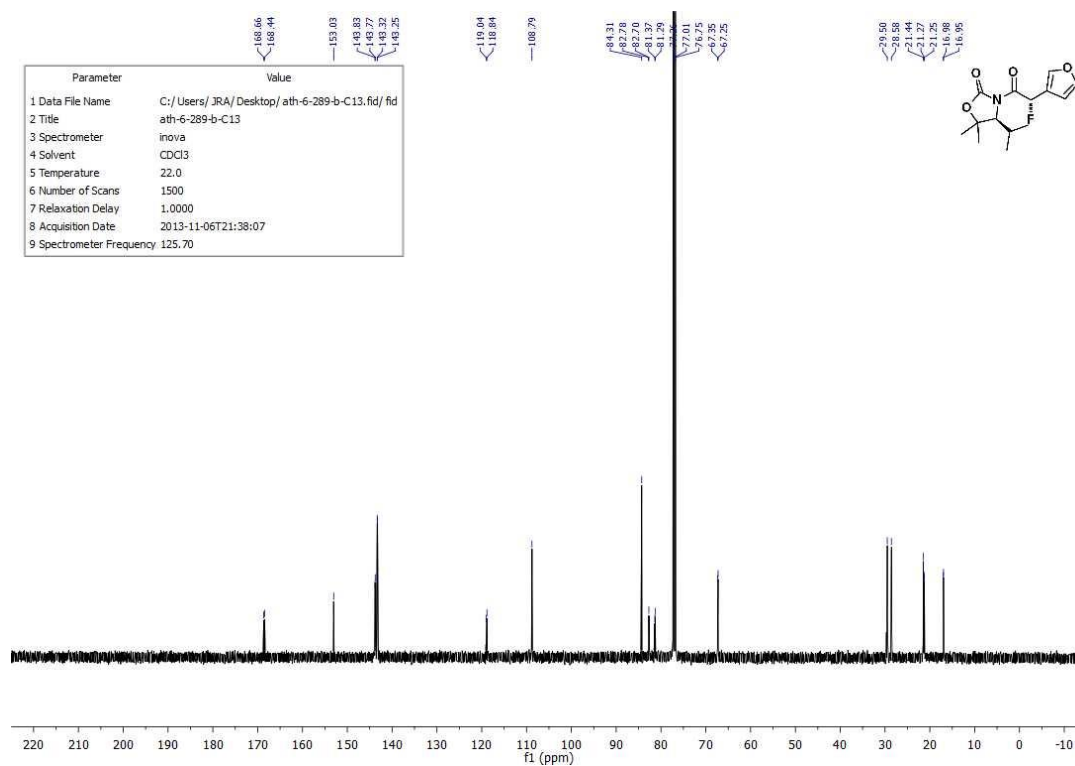
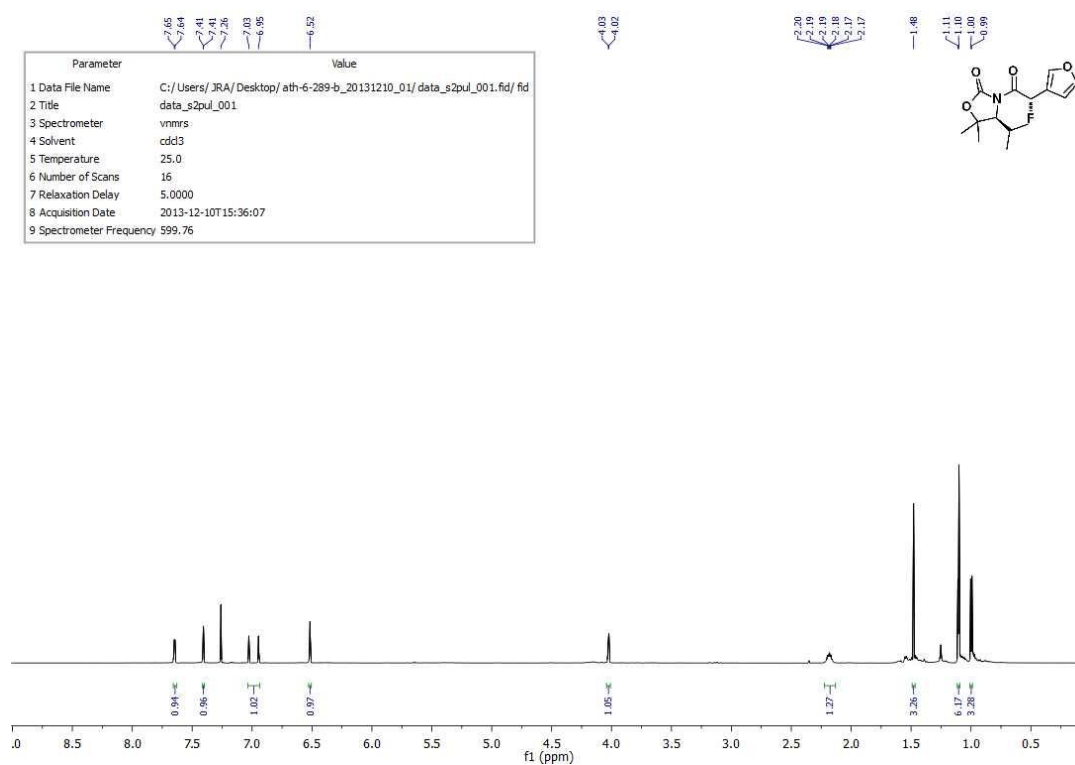


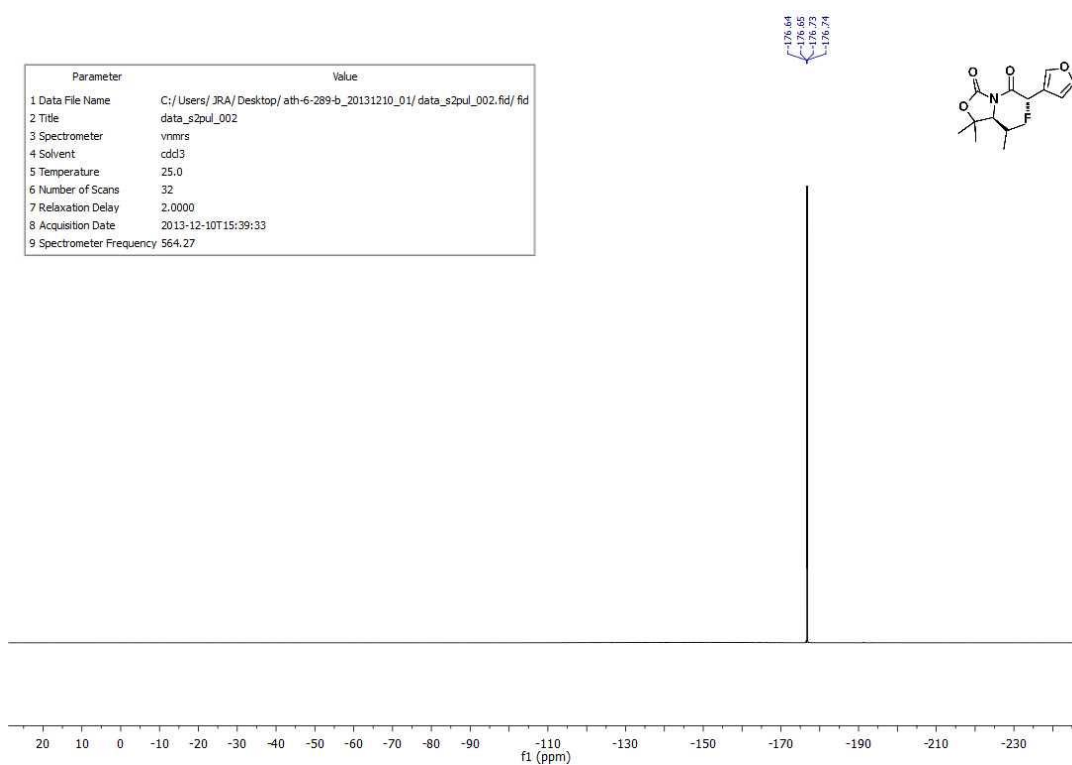
Parameter	Value
1 Data File Name	C:/Users/JRA/Desktop/JRA-4-057-b_20131210_01/F19_s2pul_JRA-4-057-b_02.fid/ fid
2 Title	F19_s2pul_JRA-4-057-b_02
3 Spectrometer	nmrns
4 Solvent	cdcl3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-12-10T19:27:30
9 Spectrometer Frequency	564.27

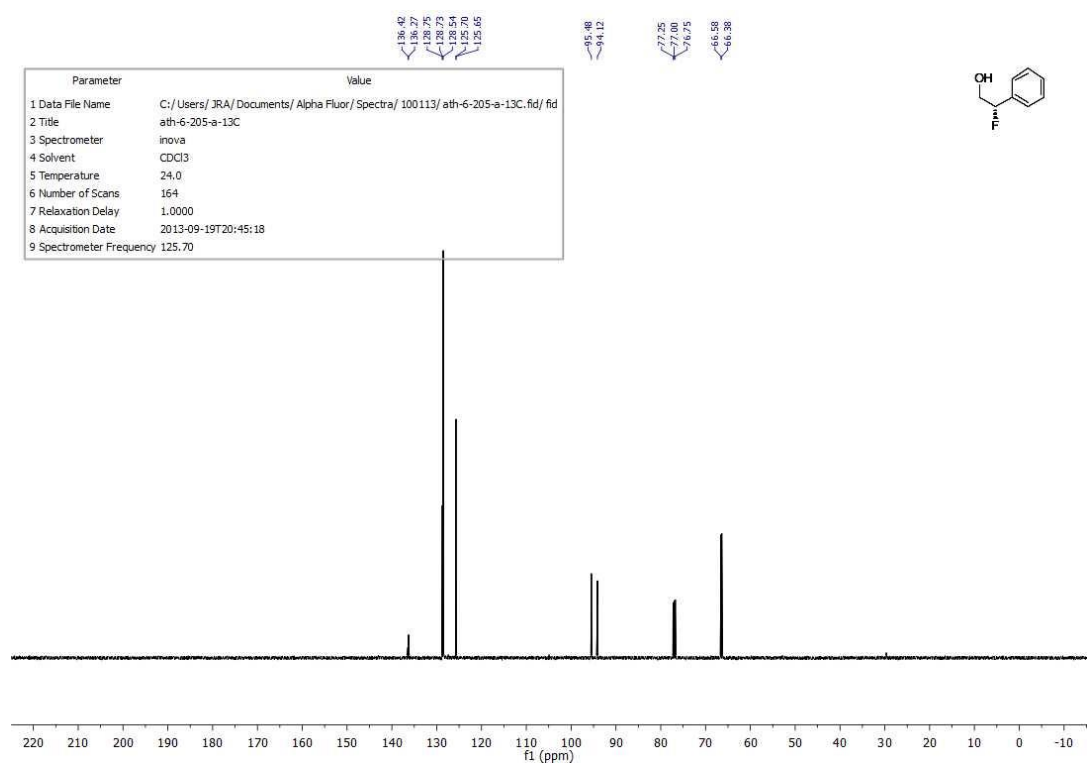
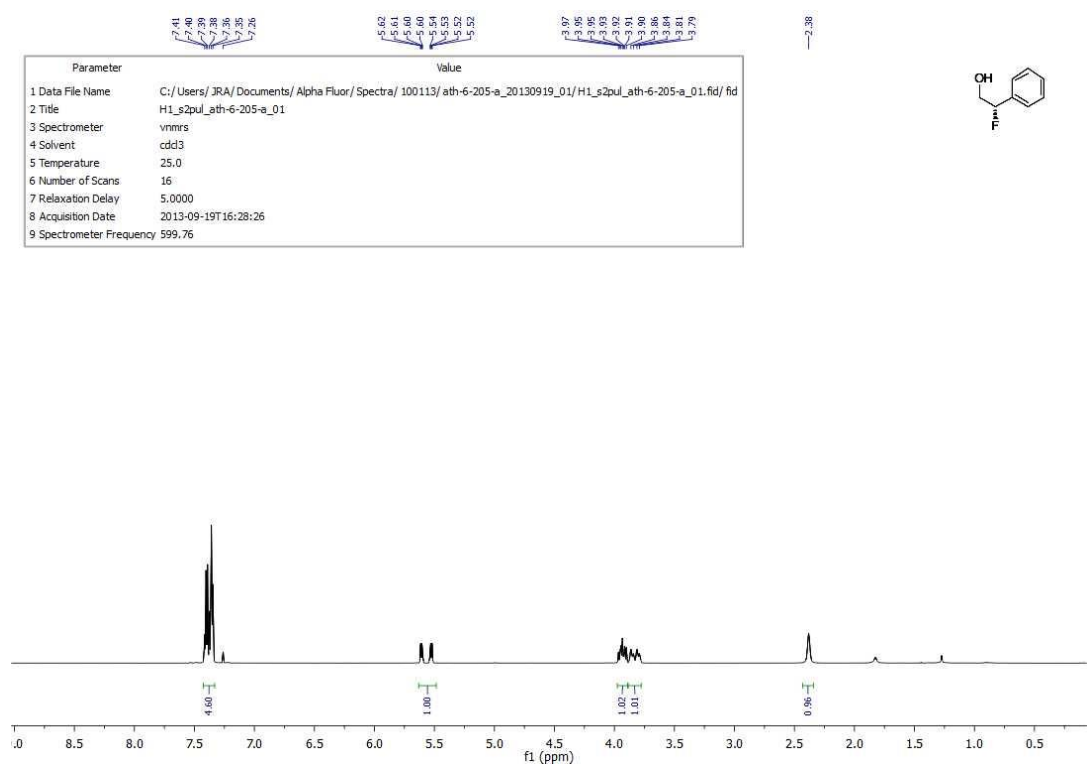






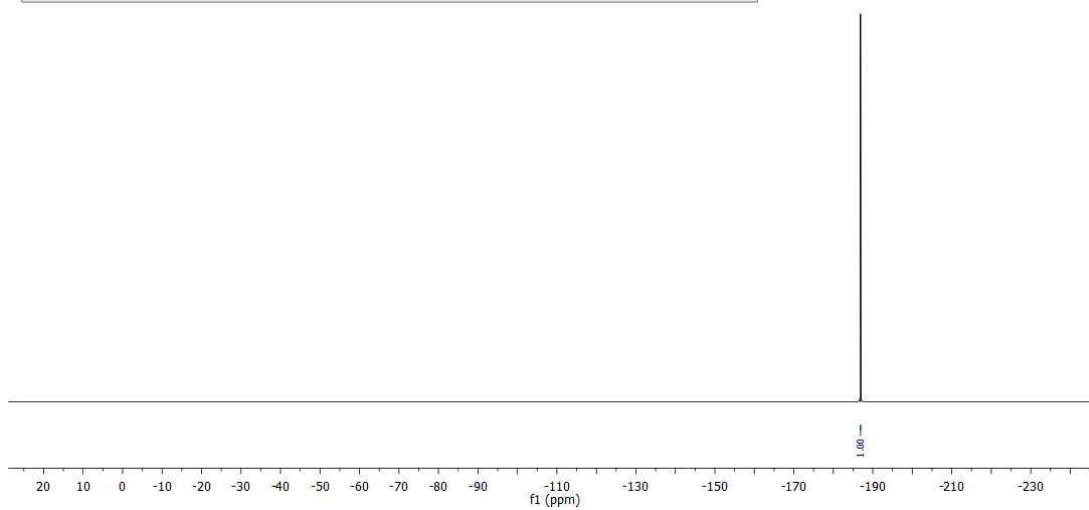


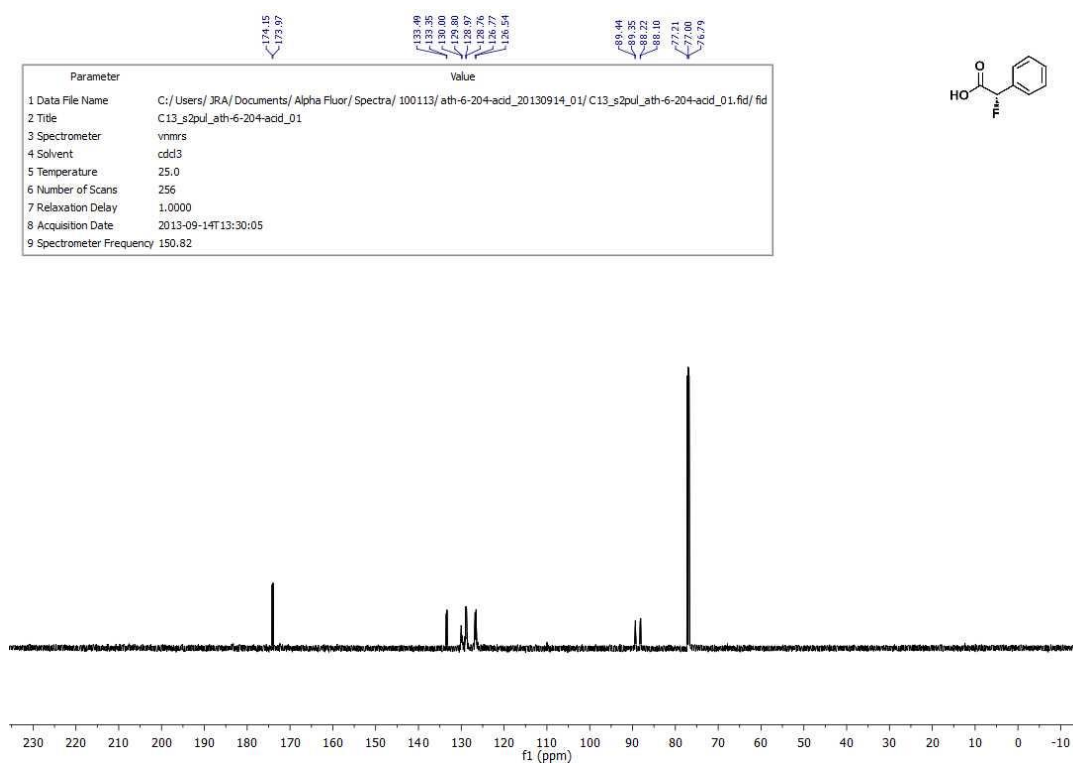
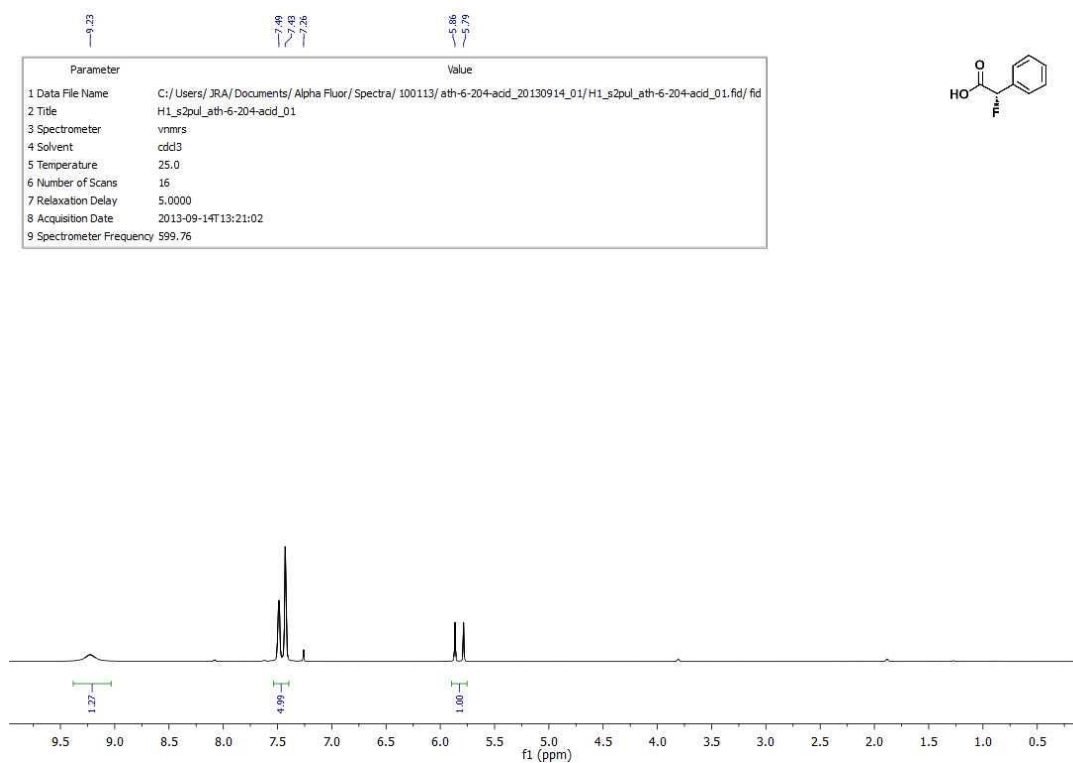


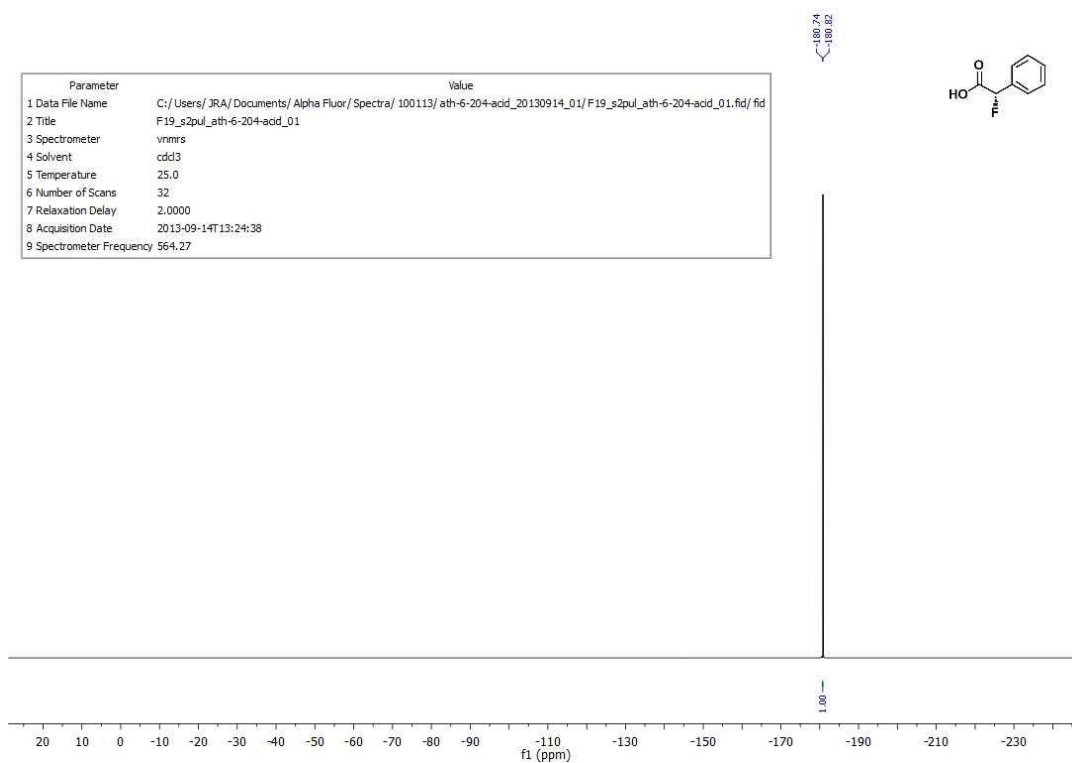


Parameter	Value
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2 Title	F19_s2pul_ath-6-205-a_01
3 Spectrometer	nmrs
4 Solvent	cdd3
5 Temperature	25.0
6 Number of Scans	32
7 Relaxation Delay	2.0000
8 Acquisition Date	2013-09-19T16:32:49
9 Spectrometer Frequency	564.27

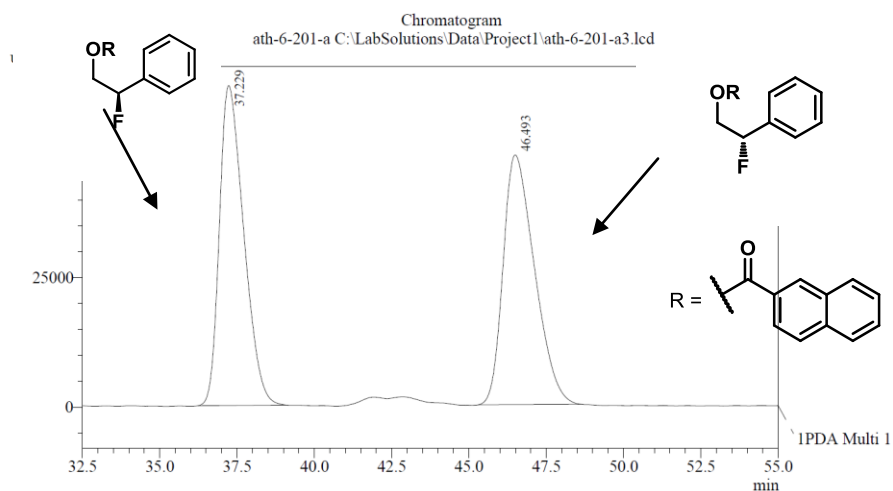
186.80
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186.89
186.92
186.94
186.97





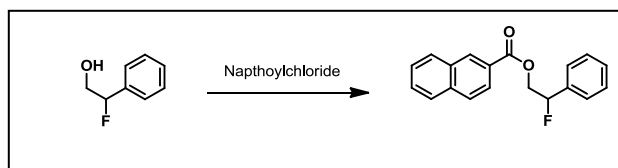


==== Shimadzu Lcsolution Analysis Report ====

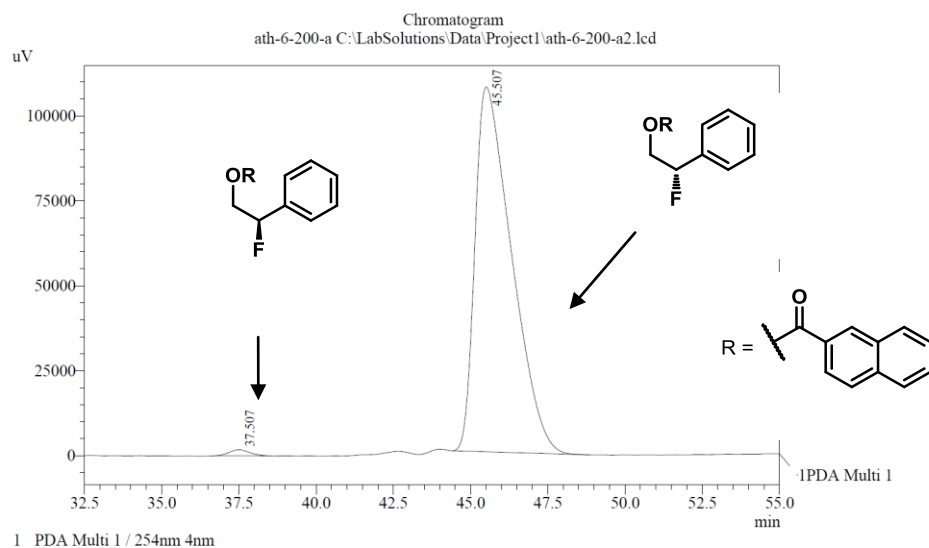


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.229	3382273	61707	49.812	56.156
2	46.493	3407826	48178	50.188	43.844
Total		6790099	109886	100.000	100.000

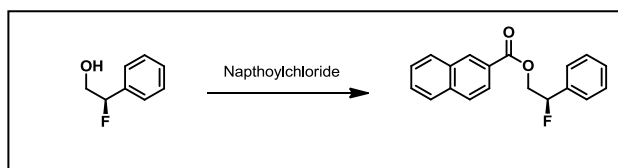


==== Shimadzu LCsolution Analysis Report =====

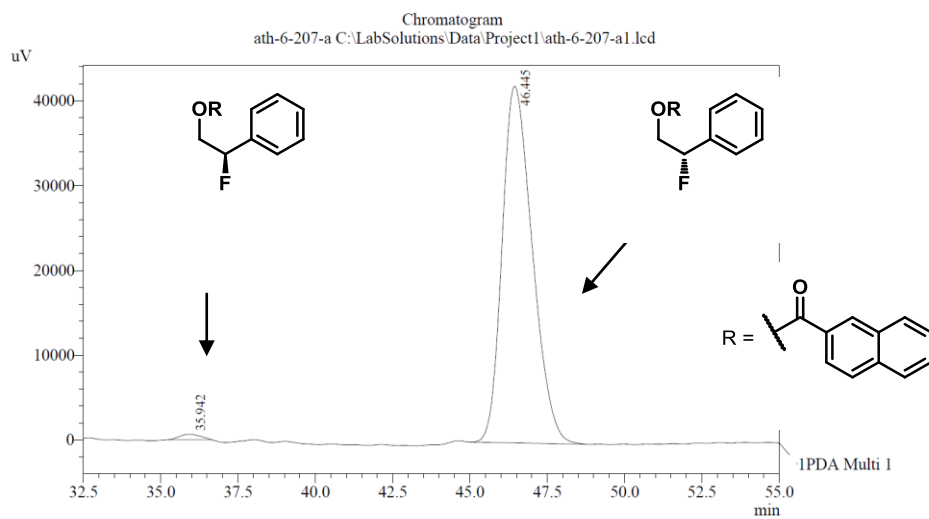


PeakTable

Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.507	79489	1751	0.890	1.604
2	45.507	8851735	107379	99.110	98.396
Total		8931224	109130	100.000	100.000



==== Shimadzu LCsolution Analysis Report =====

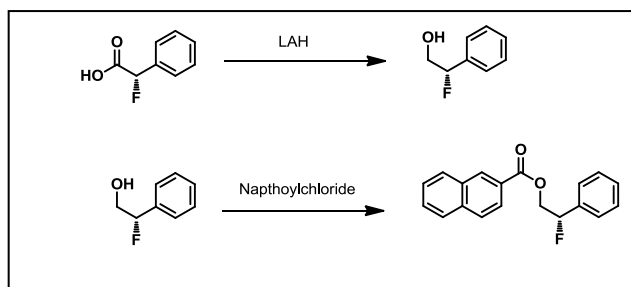


1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

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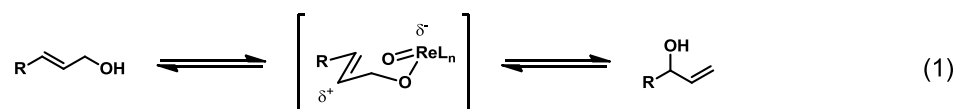


Chapter 4

Regio- and Stereocontrol in Rhenium-Catalyzed Transposition of Allylic Alcohols

4-1: Introduction

Direct catalytic transposition of allylic alcohols is a powerful approach to the synthesis of complex hydroxylated organic compounds.¹²⁶ Several transition metal catalysts have been developed for this purpose, including vanadium,¹²⁷ molybdenum,¹²⁷ and rhenium reagents.¹²⁸ Among these, rhenium(VII) oxide and triphenylsilyl perrhenate have been found to be superior in terms of reactivity and chemoselectivity, displaying high activity at low temperatures with no competitive oxidation observed with some of the other catalysts. One drawback of the reversible process (eq 1) is a general lack of regioselectivity;¹²⁹ stereoselectivity in the transposition of primary allylic alcohols is also low.



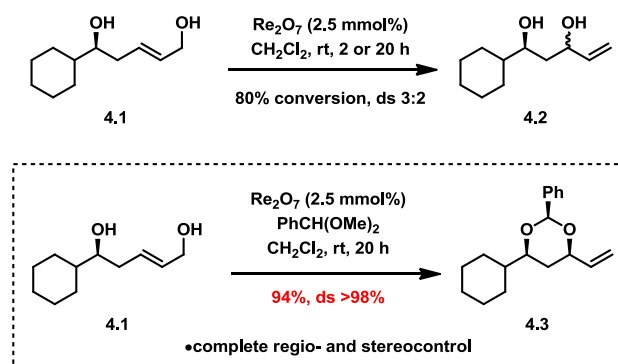
We describe a practical method that allows for control of the regio- and stereoselectivity in the rhenium-catalyzed transposition of allylic alcohols, expanding the scope of the reaction for the stereoselective synthesis of complex molecules.¹³⁰

4-2: Initial Screen and Reaction Optimization

In our initial experiments, rearrangement of substrate **4.1** in the presence of Re_2O_7 (2.5 mol %) occurred with low regio- and stereoselectivity as expected, delivering **4.2** with 60% conversion as a 3:2 mixture of diastereomers (Scheme 4.2.1). We hypothesized that the

reaction medium must be slightly acidic due to formation of a catalytic amount of perhenic acid ($pK_a = 1.25$)¹³¹ upon interaction of rhenium(VII) oxide with the substrate and/or adventitious water.¹³² In the presence of a catalytic acid the rearranged product can in principle be trapped as an acetal or ketal, and then the 1,3-*syn* diastereomer should be favored on thermodynamic grounds. Remarkably, upon exposure of **4.1** to benzaldehyde dimethyl acetal and Re_2O_7 (2.5 mol %), essentially a single product was formed in 94% yield after 20 h at room temperature. Thus, the rhenium catalyst performs a dual catalytic function as a transition metal catalyst for the hydroxyl group transposition and as an acid catalyst for acetal formation.

Scheme 4.2.1 Re-Catalyzed Transposition of **4.1**



Screening of the reaction parameters demonstrated that although a number of solvents can be used (toluene, Et_2O , THF, CH_2Cl_2),¹³³ dichloromethane provides the best results in terms of reaction rate. Typically, reactions are characterized by a rapid formation of a diastereomeric mixture of rearranged diol acetals (within ~20 min at room temperature) followed by slow equilibration of the acetals to the 1,3-*syn* product (**4.3**).

The influence of reaction time with alternative rhenium catalysts is summarized in Table 4.2.1. With all three catalysts studied, methyltrioxorhenium (MTO), $\text{Ph}_3\text{SiOReO}_3$, and

Re₂O₇, the rearrangement/acetalization was complete within 3 h at room temperature. As expected, MTO is the least reactive catalyst.^{127c,134} Notably, with *all* of the three rhenium catalysts the initial acetal formation was followed by equilibration to **4.3**. The highest rate of equilibration was observed with Re₂O₇, generating **4.3** with >98% selectivity after 20 h. With Ph₃SiOReO₃, a high level of selectivity (96:4) was also reached after 20 h at room temperature.

Table 4.2.1 Influence of the Catalyst and Reaction Time

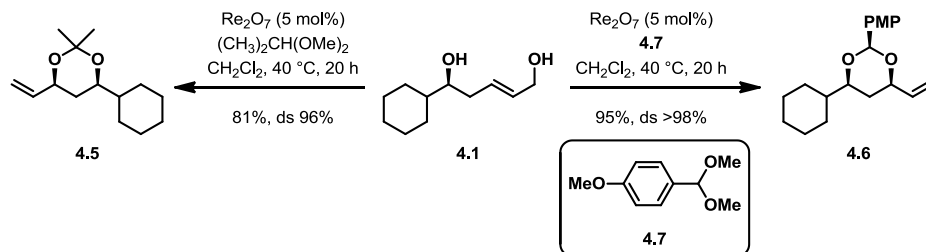
Reaction scheme: Diol **4.1** (cyclohexyl-CH(OH)-CH₂-CH=CH₂) reacts with catalyst PhCH(OMe)₂ in CH₂Cl₂ at room temperature to form a mixture of acetals **4.2** and **4.3**.

Entry	Catalyst (mol %)	Time	Conversion ^a (%)	4.2:4.3 ^a
1	MeReO ₃ (5)	40 min	45	36:64
2	MeReO ₃ (5)	3 h	100	40:60
3	MeReO ₃ (5)	20 h	100	63:37
4	Ph ₃ SiOReO ₃ (5)	40 min	100	65:35
5	Ph ₃ SiOReO ₃ (5)	3 h	100	87:13
6	Ph ₃ SiOReO ₃ (5)	20 h	100	96:4
7	Re ₂ O ₇ (2.5)	40 min	100	80:20
8	Re ₂ O ₇ (2.5)	3 h	100	91:9
9	Re₂O₇ (2.5)	20 h	100	>98:2

(a) Measured by 500 MHz NMR spectroscopy using a crude mixture of products.

As illustrated in Scheme 4.1.2, the highly stereo- and regioselective transposition can be achieved with other commonly employed diol masking groups. Acetonide formation occurred in an 81% yield (96% ds), and the *p*-methoxyphenyl (PMP) acetal **4.6** was isolated in a 95% yield with greater than 98% diastereoselectivity.

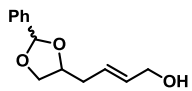
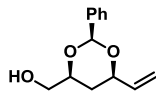
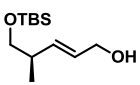
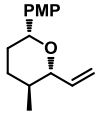
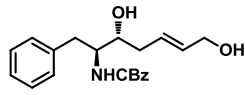
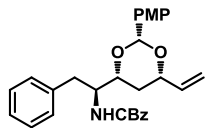
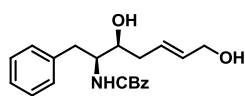
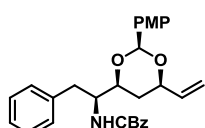
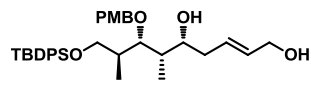
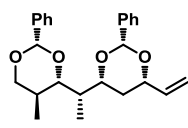
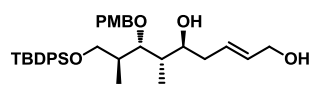
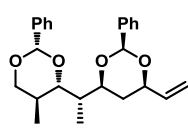
Scheme 4.2.2 Formation of the Acetonide and PMP-Acetals



4-3: Substrate Scope

The reaction scope with a range of substrates of higher complexity was explored next (Table 4.3.1). Migration of the resident benzylidene group accompanying the transposition was possible as illustrated in entry 1 (Table 4.3.1). Desilylation can be accomplished simultaneously without a need for an additional step (Table 4.3.1, entry 2). A Cbz-protected primary amine is compatible with the reaction conditions, and the relative stereochemistry of the amino alcohol has no influence on the stereoselectivity of the reaction (Table 4.3.1, entries 3, 4). Upon prolonged exposure (20 h), a complete removal of acid sensitive PMB and TBDPS groups was observed, which were replaced with the benzylidene acetal (Table 4.3.1, entries 5, 6). A more oxidized *p*-methoxybenzoyl (MBz) group and shorter reaction times (4 h) resulted in a much improved conservation of the original protecting groups (Table 4.3.2, entries 1, 2). Functionalized tetrahydropyran substrates underwent the transposition reaction with the generally observed high regiocontrol and high stereoselectivity (Table 4.3.2, entries 3, 4). Thermodynamically disfavored 1,1-disubstituted alkenes can be readily prepared in high yield (Table 4.3.2, entry 5).

Table 4.3.1 Scope of the Re-Catalyzed Transposition/Acetalization with Complex Substrates^a

Entry	Substrates	Product	yield, dr
1			80%, 96:4
2			84%, 85:15
3			65%, >98:2
4			71%, >98:2
5			79%, >98:2
6			84%, >98:2

(a) Reactions were performed in CH₂Cl₂ (~0.2 M) with 2.5 mol % of Re₂O₇ and 2.0 equiv of PhCH(OMe)₂ or 4-MeOPhCH(OMe)₂; dr is determined by 500 MHz ¹H NMR.

Table 4.3.2 Scope of the Re-Catalyzed Transposition/Acetalization with Complex Substrates^a

Entry	Substrates	Product	yield, dr
1			76%, ^b >98:2
2			84%, ^b >98:2
3			81%, 96:4
4			82%, ^c >98:2
5			97%, >98:2

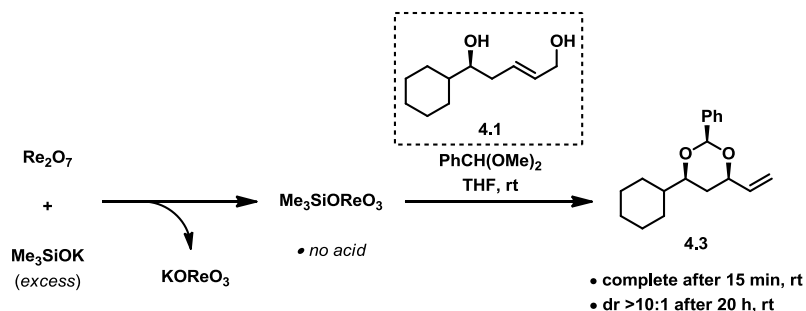
(a) Reactions were performed in CH₂Cl₂ (~0.2 M) with 2.5 mol % of Re₂O₇ and 2.0 equiv of PhCH(OMe)₂ or 4-MeOPhCH(OMe)₂; dr is determined by 500 MHz ¹H NMR. (b) Overall yield after treatment with TBAF. (c) R=H/R=TBS 5.3:1.

An intriguing aspect of the reaction is that the transposition and acetalization are typically complete in an initially nonstereoselective manner within minutes (less than 30 min), followed by relatively slow isomerization to the preferred stereoisomer. In a control experiment, when a 6:3:1 diastereomeric mixture of benzylidene acetals **4.4** was subjected to the standard reaction conditions (dry CH₂Cl₂, argon atmosphere, 2.5 mol % Re₂O₇, rt, 20 h), a single stereoisomer (**4.3**) was isolated in 90% yield. In contrast, treatment of the same

mixture with *p*-TsOH (5 mol %, dry CH₂Cl₂, argon atmosphere, rt, 21 h) resulted in no change.

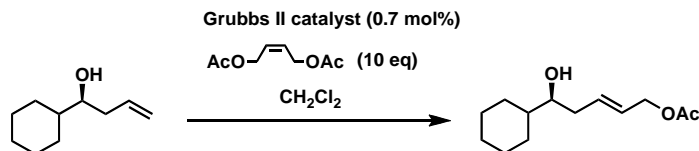
As was also noted by Grubbs and Rychnovsky,^{128b,131} addition of 0.2 equiv of 2,6-di-*tert*-butyl-4-methylpyridine (DTMP) completely suppressed the transposition and acetalization with either Re₂O₇ or Ph₃SiOReO₃. Addition of Bu₄NOAc or a proton sponge also suppressed the reaction. These results may be explained either by increasing the pH of the medium or by a modification of the catalyst through irreversible complexation.^{128b,131} To conclusively establish reactivity in the absence of acid or alternative ligands, we prepared the catalyst in situ using an excess of strongly basic Me₃SiOK (0.35 equiv) and Re₂O₇ (0.20 equiv) in THF.¹³⁵ As shown in Scheme 4.3.1, the system maintained full catalytic activity, indicating a possibility where the acetal formation is likely due to the Lewis acidic character of trimethylsilyl perrhenate.

Scheme 4.3.1 Reactivity in the Absence of a Brønsted Acid



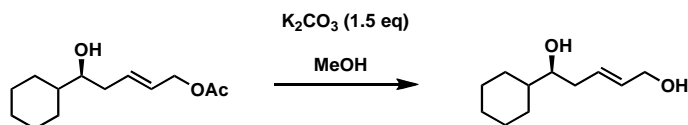
In summary, we developed a method that allows the control of regio- and stereoselectivity by a neighboring hydroxyl group in the Re-catalyzed transposition of allylic alcohols with accompanying formation of acetals.

4-4: Rhenium-Catalyzed Transposition of Allylic Alcohols Supporting Information

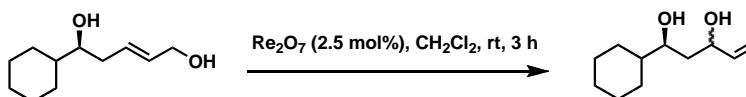


Typical procedure for cross metathesis: (*E*)-5-Cyclohexyl-5-hydroxypent-2-enyl acetate.

Grubbs II catalyst (0.116 g, 0.136 mmol) was added to a solution of the substrate¹³⁶ (3.00 g, 19.4 mmol) and *cis*-1,4-diacetoxy-2-butene (33.5 g, 0.19 mol) in degassed dichloromethane (280 ml). The reaction vessel was sealed and heated at 40 °C. After 4 h, the reaction vessel was removed from the oil bath and continued to stir at room temperature for 12 h. The reaction was concentrated on a rotary evaporator, and *cis*-1,4-diacetoxy-2-butene was distilled off. The 500 MHz ¹H NMR of the crude mixture indicated a 5:1 selectivity favoring the *E*-isomer. The residue was purified by column chromatography (silica, 15% (500 ml) to 20% (500 ml) to 30% EtOAc – hexanes) delivering the product (3.51 g, 15.5 mmol, 80%). ¹H NMR (500 MHz, CDCl₃); δ(ppm): 5.81 (ddd, J₁=15.0 Hz, J₂=J₃=6.5 Hz, 1H); 5.67 (ddd, J₁=15.0 Hz, J₂=J₃=6.0 Hz, 1H); 4.54 (d, J=6.0 Hz, 2H); 3.40 (bs, 1H); 2.34-2.28 (m, 1H); 2.19-2.11 (m, 1H); 2.06 (m, 3H); 1.84 (d, J=12.0 Hz, 1H); 1.80-1.72 (m, 2H); 1.68-1.61 (m, 2H); 1.51 (bs, 1H); 1.38-1.31 (m, 1H); 1.28-0.97 (m, 5H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 171.1, 132.9, 127.3, 75.2, 65.2, 43.4, 37.4, 29.3, 28.2, 26.7, 26.5, 26.3, 21.2. HRMS (ESI) calcd for C₁₃H₂₂O₃Na [M+Na] 249.1467, found 249.1474.

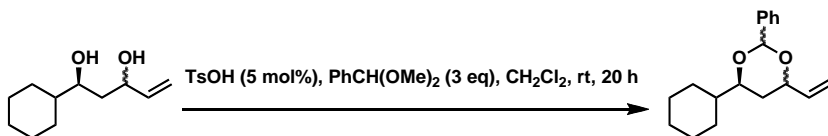


Typical procedure for deacetylation: (E)-5-Cyclohexylpent-2-ene-1,5-diol. Potassium carbonate (3.22 g, 23.3 mmol) was added to a solution of the substrate (3.51 g, 15.5 mmol) in methanol (78 ml) at 0 °C. After 10 min, the reaction was warmed to rt and continued to stir for 1 h 20 min. Dilute with water and ethyl acetate. The mixture was extracted with ethyl acetate (4x30 ml), and the organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 60% to 80% to 100% EtOAc – hexanes) delivering the product (2.52 g, 13.7 mmol, 88%). IR (cm^{-1}) 3306.4, 2925.5, 1668.1, 1095.4; ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 5.79-5.70 (m, 2H); 4.16-4.10 (m, 2H); 3.42-3.37 (m, 1H); 2.34-2.29 (m, 1H); 2.17-2.11 (m, 1H); 1.87-1.82 (m, 1H); 1.79-1.74 (m, 2H); 1.70-1.64 (m, 2H); 1.53 (bs, 1H); 1.45-1.40 (m, 1H); 1.39-1.32 (m, 1H); 1.29-0.97 (m, 5H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 132.3, 129.6, 75.4, 63.4, 43.4, 37.2, 29.2, 28.4, 26.7, 26.4, 26.3. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]$ 207.1361, found 207.1356.

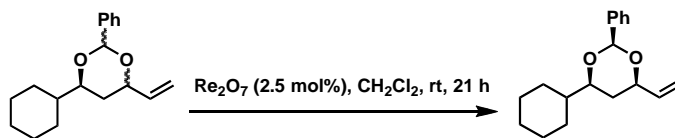


1-Cyclohexylpent-4-ene-1,3-diol, mixture of diastereomers. Rhenium(VII) oxide (6 mg, 0.013 mmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). Dichloromethane (2 ml) was added to the flask. The substrate (92 mg, 0.50 mmol) in dichloromethane (3 ml total with rinses) was added to the reaction vessel. After 3 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture was stirred vigorously for 10 min. The aqueous layer was extracted with

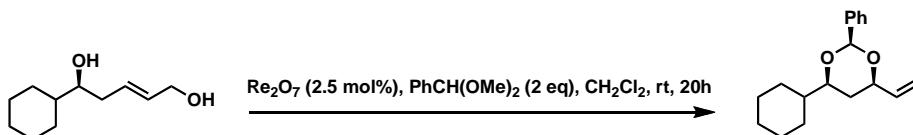
dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 40% EtOAc – hexanes) delivering the product (55.3 mg, 0.300 mmol, 60%). The remaining starting material was not collected. ^1H NMR (500 MHz, CDCl_3); δ (ppm): 5.94 (ddd, $J_1=17.0$ Hz, $J_2=10.5$ Hz, $J_3=5.5$ Hz, 0.4H); 5.89 (ddd, $J_1=17.5$ Hz, $J_2=10.5$ Hz, $J_3=6.5$ Hz, 0.6H); 5.30 (ddd, $J=17.0$ Hz, $J_2=J_3=1.5$ Hz, 0.4H); 5.26 (ddd, $J_1=17.5$ Hz, $J_2=J_3=1.5$ Hz, 0.6H); 5.14 (ddd, $J_1=11.0$ Hz, $J_2=J_3=1.5$ Hz, 0.4H); 5.10 (ddd, $J_1=10.5$ Hz, $J_2=1.5$ Hz, 0.6H); 4.47 (bs, 0.4H); 4.36 (bs, 0.6H); 3.72-3.64 (m, 1H); 2.95 (s, 0.6H); 2.63 (s, 0.6H); 2.50 (d, $J=4.5$ Hz, 0.4H); 2.11 (d, $J=3.5$ Hz, 0.4H); 1.86-1.53 (m, 7H); 1.39-1.31 (m, 1H); 1.28-0.95 (m, 5H). LRMS (ESI) calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]$ 207, found 207.



4-Cyclohexyl-2-phenyl-6-vinyl-1,3-dioxane, mixture of diastereomers. *p*-Toluenesulfonic acid (3 mg, 0.015 mmol) was added to a solution of the substrate (55 mg, 0.300 mmol), and benzaldehyde dimethyl acetal (0.14 ml, 0.90 mmol) in dichloromethane (3.0 ml). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% EtOAc – hexanes) delivering the product (65.5 mg, 0.240 mmol, 80%) as a 6:3:1 mixture of three diastereomers as determined by 500 MHz ^1H NMR.



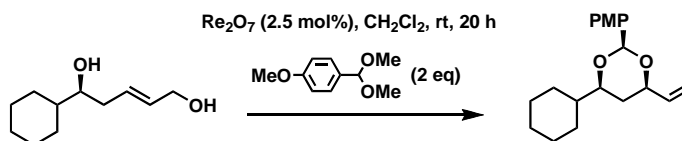
***cis,cis*-4-Cyclohexyl-2-phenyl-6-vinyl-1,3-dioxane.** Rhenium(VII) oxide (6.7 mg, 13.7 μ mol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). Dichloromethane (2.5 ml) was added to the flask. The substrate (0.150 g, 0.551 mmol) in dichloromethane (3 ml total with rinses) was added to the reaction vessel. After 21 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% EtOAc – hexanes) delivering the product (0.136 mg, 0.498 mmol, 90%). IR (cm^{-1}) 3423.0, 3035.4, 2926.5, 1451.17, 1273.6; ^1H NMR (500 MHz, CDCl_3); δ (ppm): 7.55-7.53 (m, 2H); 7.38-7.30 (m, 3H); 5.95 (ddd, $J_1=17.0$ Hz, $J_2=10.5$ Hz, $J_3=5.5$ Hz, 1H); 5.57 (s, 1H); 5.35 (ddd, $J_1=17.5$ Hz, $J_2=J_3=1.5$ Hz, 1H); 5.17 (ddd, $J_1=11.0$ Hz, $J_2=J_3=1.5$ Hz, 1H); 4.33 (dddd, $J_1=10.0$ Hz, $J_2=5.5$ Hz, $J_3=3.0$ Hz, $J_4=1.5$ Hz, 1H); 3.59 (ddd, $J_1=11.0$ Hz, $J_2=7.0$ Hz, $J_3=2.5$ Hz, 1H); 2.04-2.02 (m, 1H); 1.78-1.75 (m, 3H); 1.70-1.67 (m, 2H); 1.57-1.50 (m, 2H); 1.30-1.13 (m, 3H); 1.11-1.01 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3); δ (ppm): 139.2, 138.4, 128.7, 128.3, 126.4, 115.5, 100.7, 81.2, 77.7, 42.8, 34.2, 29.1, 28.4, 26.8, 26.3, 26.2. HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2\text{Na}$ [$\text{M}+\text{Na}$] 295.1674, found 295.1674.



Typical procedure for the stereoselective Re-catalyzed transposition/ acetalization:

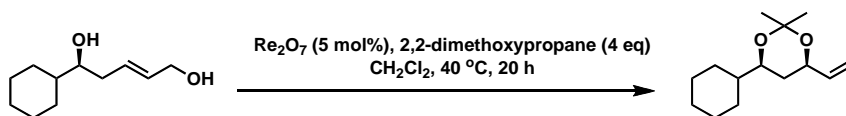
***cis,cis*-4-Cyclohexyl-2-phenyl-6-vinyl-1,3-dioxane.** Rhenium(VII) oxide (12 mg, 0.025 mmol)

was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3), and dichloromethane (5 ml) was added. The substrate (0.184 g, 1.00 mmol) in dichloromethane (5 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (0.30 ml, 2.00 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% EtOAc – hexanes) delivering the product (0.255 g, 0.936 mmol, 94%). IR (cm⁻¹) 3423.0, 3035.4, 2926.5, 1451.17, 1273.6; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.55-7.53 (m, 2H); 7.38-7.30 (m, 3H); 5.95 (ddd, J1=17.0 Hz, J2=10.5 Hz, J3=5.5 Hz, 1H); 5.57 (s, 1H); 5.35 (ddd, J1=17.5 Hz, J2=J3=1.5 Hz, 1H); 5.17 (ddd, J1=11.0 Hz, J2=J3=1.5 Hz, 1H); 4.33 (dddd, J1=10.0 Hz, J2=5.5 Hz, J3=3.0 Hz, J4=1.5 Hz, 1H); 3.59 (ddd, J1= 11.0 Hz, J2=7.0 Hz, J3=2.5 Hz, 1H); 2.04-2.02 (m, 1H); 1.78-1.75 (m, 3H); 1.70-1.67 (m, 2H); 1.57-1.50 (m, 2H); 1.30-1.13 (m, 3H); 1.11-1.01 (m, 2H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 139.2, 138.4, 128.7, 128.3, 126.4, 115.5, 100.7, 81.2, 77.7, 42.8, 34.2, 29.1, 28.4, 26.8, 26.3, 26.2. HRMS (ESI) calcd for C₁₈H₂₄O₂Na [M+Na] 295.1674, found 295.1674.



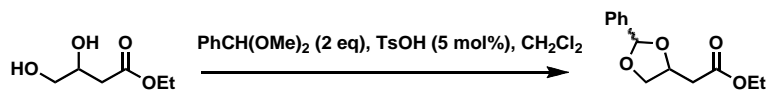
***cis,cis*-4-Cyclohexyl-2-(4-methoxyphenyl)-6-vinyl-1,3-dioxane.** Rhenium(VII) oxide (12 mg, 0.025 mmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (5 ml). The substrate (0.184 g, 1.00 mmol) in dichloromethane (5 ml total with rinses) was added to the reaction vessel

followed by addition of anisaldehyde dimethyl acetal (0.34 ml, 2.00 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% EtOAc – hexanes) delivering the product (0.285 g, 0.942 mmol, 94%). IR (cm⁻¹) 2926.5, 1615.1, 1517.7, 1248.7; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.47-7.43 (m, 2H); 6.89-6.87 (m, 2H); 5.94 (ddd, J1=17.5 Hz, J2=10.5 Hz, J3=5.5 Hz, 1H); 5.52 (s, 1H); 5.33 (ddd, J1=17.5 Hz, J2=J3=1.5 Hz, 1H) 5.15 (ddd, J1=10.5 Hz, J2=J3=1.5 Hz, 1H); 4.30 (dddd, J1=9.5 Hz, J2=5.5 Hz, J3=2.5 Hz, J4=1.0 Hz, 1H); 3.80 (s, 3H); 3.57 (ddd, J1=11.5 Hz, J2=7.0 Hz, J3=2.5 Hz, 1H); 2.0 (bd, J=13.0 Hz, 1H); 1.77-1.71 (m, 3H); 1.70-1.64 (m, 2H); 1.55-1.48 (m, 2H); 1.30-1.12 (m, 3H); 1.10-0.98 (m, 2H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 159.9, 138.4, 131.8, 127.6, 115.5, 113.7, 100.6, 81.1, 77.6, 55.5, 42.8, 34.1, 29.0, 28.4, 26.8, 26.3, 26.2. HRMS (ESI) calcd for C₁₉H₂₆O₃Na [M+Na] 325.1780, found 325.1791.



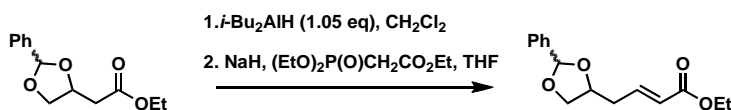
cis-4-Cyclohexyl-2,2-dimethyl-6-vinyl-1,3-dioxane. Rhenium(VII) oxide (24 mg, 0.050 mmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). Dichloromethane (5 ml) was added to the flask. The substrate (0.184 g, 1.00 mmol) in dichloromethane (5 ml total with rinses) was added to the reaction vessel followed by addition of 2,2-dimethoxypropane (0.60 ml, 4.00 mmol). The reaction vessel was sealed and heated at 40 °C. After 20 h, the reaction vessel was allowed to cool to room temperature, and saturated aqueous sodium bicarbonate was added. The biphasic mixture stirred vigorously for 10

min. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% EtOAc – hexanes) delivering the product (0.182 g, 0.811 mmol, 81%). IR (cm⁻¹) 2924.5, 1645.0, 1026.9; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 5.83 (ddd, J1=16.5 Hz, J2=10.0 Hz, J3=5.5 Hz, 1H); 5.25 (ddd, J1=17.0 Hz, J2=J3=1.0 Hz, 1H); 5.11 (ddd, J1=10.5 Hz, J2=J3=1.0 Hz, 1H); 4.31 (dddd, J1=10.0 Hz, J2=6.0 Hz, J3=2.5 Hz, J4=1.5 Hz, 1H); 3.57 (ddd, J1=11.5 Hz, J2=7.0 Hz, J3=2.5 Hz, 1H); 1.94-1.88 (m, 1H); 1.75-1.64 (m, 4H); 1.53 (ddd, J1=13.0 Hz, J2=J3=3.0 Hz, 1H); 1.45 (s, 3H); 1.41 (s, 3H); 1.37-1.09 (m, 5H); 0.99-0.88 (m, 2H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 139.3, 115.4, 98.7, 73.2, 70.7, 43.0, 34.1, 30.5, 29.1, 28.2, 26.9, 26.3, 26.2, 20.0. LRMS (CI) calcd for C₁₄H₂₄O₂Na [M+H] 225, found 225.



Ethyl 2-(2-phenyl-1,3-dioxolan-4-yl)acetate. *p*-Toluenesulfonic acid (0.118 g, 12.4 mmol) was added to a solution of the substrate¹³⁷ (1.84 g, 12.4 mmol) and benzaldehyde dimethyl acetal (5.60 ml, 37.2 mmol) in dichloromethane (41 ml) at rt. After 30 min, saturated aqueous sodium bicarbonate was added. The aqueous layer was extracted with dichloromethane (2x30 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% → 20% EtOAc – hexanes) delivering the product (1.80 g, 7.62 mmol, 61%). IR (cm⁻¹) 3064.3, 2935.1, 1717.3, 1654.6, 1602.6, 1273.8; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.49-7.45 (m, 2H); 7.41-7.35 (m, 3H); 5.95 (s, 0.5H); 5.81 (s, 0.5H); 4.66-4.60 (m, 1H); 4.37 (dd, J1=8.0 Hz, J2=5.5 Hz, 0.5H); 4.222 (dd, J1=8.5 Hz, J2=6.5 Hz, 0.5H); 4.20-4.13 (m, 2H); 3.87 (dd, J1=8.0 Hz, J2=5.5 Hz, 0.5H); 3.75 (dd, J1=8.5 Hz, J2=6.5 Hz, 0.5H); 2.85 (dd, J1=16.0 Hz, J2=6.0 Hz, 1H); 2.63 (ddd, J1=16.0 Hz, J2=J3=8.0 Hz,

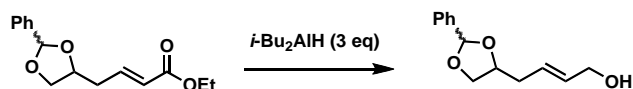
1H); 1.28 (dd, J1=J2=6.5 Hz, 1.5H); 1.27 (dd, J1=J2=7.0 Hz, 1.5H). LRMS (ESI) calcd for C₁₃H₁₆O₄Na [M+Na] 259.1, found 259.1.



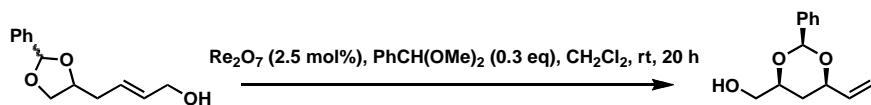
(E)-Ethyl 4-(2-phenyl-1,3-dioxolan-4-yl)but-2-enoate. Diisobutylaluminum hydride (1 M in toluene, 6.45 ml, 6.44 mmol) was added to a solution of the substrate (1.45 g, 6.13 mmol) in dichloromethane (30.6 ml) at -78 °C over 30 min. The reaction was allowed to stir at -78 °C for an additional 30 min before being quenched with a solution of Rochelle's salt at -78 °C. The mixture was stirred vigorously at rt for 2 h, the layers were separated, and the aqueous layer was extracted with dichloromethane (2x30 ml). The organic layers were dried with sodium sulfate and concentrated, and the residue was submitted to the next reaction without further purification.

To a suspension of sodium hydride (60% suspension in oil, 0.295 g, 7.36 mmol) and dry THF (20.6 ml) was added triethyl phosphonoacetate (1.85 ml, 9.19 mmol) at -10 °C, and the mixture was stirred for 30 min. A solution of the residue in THF (10 ml total with rinses) was added to the solution at -10 °C. The mixture was allowed to stir for 30 min before being quenched with saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate (3x30 ml), and the combined organic layers were washed with water and brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% EtOAc – hexanes) delivering the product (1.28 g, 4.88 mmol, 80% over 2 steps). IR (cm⁻¹) 3064.3, 2935.1, 1717.3, 1654.6, 1602.6, 1273.8; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.50-7.45 (m, 2H); 7.40-7.36 (m, 3H); 7.01-6.94 (m, 1H); 5.97-5.92 (m, 1H); 5.96 (s, 0.4H); 5.81 (s, 0.6H); 4.42-4.34 (m, 1H); 4.27 (dd, J1=8.0 Hz, J2=6.0 Hz, 0.4 H); 4.22-4.17 (m, 2H); 4.13 (dd, J1=8.0 Hz, J2=7.0 Hz, 0.6H); 3.79 (dd, J1=8.0 Hz, J2=6.0 Hz, 0.6H); 3.69 (dd, J1=8.0 Hz, J2=7.0 Hz,

0.4H); 2.68-2.61 (m, 1H); 2.58-2.49 (m, 1H); 1.30-1.26 (m, 3H). LRMS (ESI) calcd for $C_{15}H_{18}O_4Na$ [M+Na] 285.1, found 285.1.

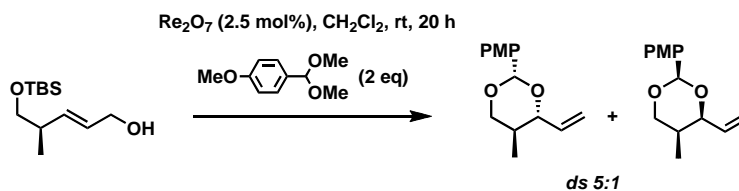


(*E*)-4-(2-phenyl-1,3-dioxolan-4-yl)but-2-en-1-ol. Diisobutylaluminum hydride (1 M in toluene, 14.5 ml, 14.5 mmol) was added to a solution of the substrate (1.27 g, 4.84 mmol) in dichloromethane (24.2 ml) at -78 °C. The reaction was allowed to warm from -78 °C to -20 °C over 1 h before being quenched with a solution of Rochelle's salt at 0 °C. The mixture was stirred vigorously for 2 h, the layers were separated, and the aqueous layer was extracted with dichloromethane (2x30 ml). The combined organic layers were dried with sodium sulfate and concentrated, and the residue was purified by column chromatography (silica, 60% → 80% ethyl acetate – hexanes) to give the desired product (0.571 g, 2.59 mmol, 54%). ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.52-7.45 (m, 2H); 7.40-7.33 (m, 3H); 5.95 (s, 1H); 5.82-5.71 (m, 2H); 4.30 (dd, J₁=8.0 Hz, J₂=6.5 Hz, 1H); 4.25-4.22 (m, 1H); 4.14-4.11 (m, 2H); 3.68 (dd, J₁=8.0 Hz, J₂=7.0 Hz, 1H); 2.52 (ddd, J₁=13.5 Hz, J₂=J₃=6.5 Hz, 1H); 2.38 (ddd, J₁=13.5 Hz, J₂=J₃=7.0 Hz, 1H); 1.36-1.30 (m, 1H). LRMS (ESI) calcd for $C_{13}H_{16}O_3Na$ [M+Na] 243.1, found 243.1.



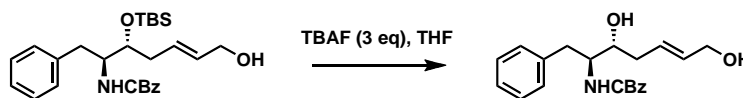
cis,cis-2-Phenyl-6-vinyl-1,3-dioxan-4-ylmethanol. The typical procedure was followed: rhenium(VII) oxide (12 mg, 0.025 mmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). Dichloromethane (2.5 ml) was added. The substrate (0.220 g, 1.00 mmol) in dichloromethane (2.5 ml total with rinses) was added to the

reaction vessel followed by addition of benzaldehyde dimethyl acetal (45 μ l, 0.30 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x20 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 35% EtOAc – hexanes) delivering the product (0.175 g, 0.795 mmol, 80%). IR (cm^{-1}) 3420.1, 3067.2, 2921.6, 1647.9, 1601.59, 1275.7; ^1H NMR (500 MHz, CDCl_3); δ (ppm): 7.54-7.52 (m, 2H); 7.40-7.34 (m, 3H); 5.95 (ddd, $J_1=17.5$ Hz, $J_2=11.0$ Hz, $J_3=5.5$ Hz, 1H); 5.63 (s, 1H); 5.36 (ddd, $J_1=17.0$ Hz, $J_2=J_3=1.5$ Hz, 1H); 5.20 (ddd, $J_1=11.0$ Hz, $J_2=J_3=1.5$ Hz, 1H); 4.40-4.36 (s, 1H); 4.05-4.00 (m, 1H); 3.74-3.68 (m, 1H); 3.65 (dd, $J_1=11.5$ Hz, $J_2=6.5$ Hz, 1H); 2.23 (bs, 1H); 1.69-1.59 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3); δ (ppm): 138.4, 137.7, 129.5, 128.5, 126.5, 116.1, 100.9, 77.3, 77.1, 65.8, 32.4. HRMS (ESI) calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3\text{Na}$ [$\text{M}+\text{Na}$] 243.0997, found 243.0993.



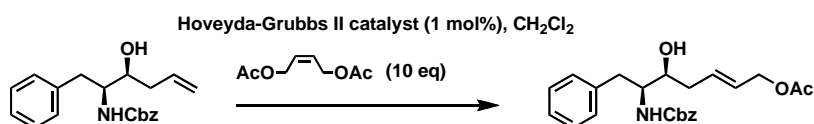
(2*S*,4*R*,5*S*)-2-(4-Methoxyphenyl)-5-methyl-4-vinyl-1,3-dioxane. Following the typical procedure, rhenium(VII) oxide (7.9 mg, 0.016 mmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (1.25 ml). The substrate¹³⁸ (0.150 g, 0.651 mmol) in dichloromethane (2.5 ml total with rinses) was added to the reaction vessel followed by addition of anisaldehyde dimethyl acetal (0.220 ml, 1.30 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was

extracted with dichloromethane (3x20 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% EtOAc – hexanes) delivering the product (0.128 g, 0.546 mmol, 84%) as a 5:1 inseparable mixture diastereomers. IR (cm⁻¹) 2958.3, 1615.1, 1518.7, 1249.7; ¹H NMR (500 MHz, CDCl₃); δ(ppm): (major diastereomer) 7.46-7.43 (m, 2H); 6.90-6.87 (m, 2H); 5.89 (ddd, J₁=17.5 Hz, J₂=10.5 Hz, J₃=7.4 Hz, 1H); 5.50 (s, 1H); 5.35 (ddd, J₁=17.5 Hz, J₂=J₃=2.0 Hz, 1H); 5.25 (ddd, J₁=10.5 Hz, J₂=1.5 Hz, J₃=0.5 Hz, 1H); 4.15 (dd, J₁=11.5 Hz, J₂=5.0 Hz, 1H); 3.87 (dd, J₁=10.0 Hz, J₂=7.0 Hz, 1H); 3.80 (s, 3H); 3.54 (dd, J₁=J₂=11.0 Hz, 1H); 1.94-1.86 (m, 1H); 0.79 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 160.1, 136.2, 131.2, 127.7, 118.1, 113.8, 101.1, 84.9, 73.1, 55.5, 34.0, 12.5. HRMS (ESI) calcd for C₁₄H₁₈O₃Na [M+Na] 257.1154, found 257.1147.

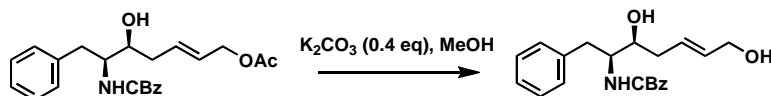


***anti*-Benzyl 3,7-dihydroxy-1-phenylhept-5-en-2-ylcarbamate.** Tetra-*n*-butyl-ammonium fluoride (1M in THF, 0.385 ml, 0.385 mmol) was added to a solution of the substrate¹³⁹ (60 mg, 0.128 mmol) in THF (0.25 ml) at room temperature. The solution was stirred at room temperature for 2 h and was quenched with a saturated solution of ammonium chloride. The aqueous layer was extracted with ethyl acetate (3x10 ml), dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 5% methanol - dichloromethane) to give the desired diol (43.1 mg, 0.121 mmol, 95%). IR (cm⁻¹) 3394.1, 3029.6, 2930.2, 1696.1, 1516.7, 1254.5; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.37-7.16 (m, 10H); 5.69 (ddd, J₁=16.0 Hz, J₂=J₃=5.5 Hz, 1H); 5.60 (ddd, J₁=15.0 Hz, J₂=J₃=6.5 Hz, 1H); 5.17 (bd, J=8.5 Hz, 1H); 5.08 (AB, J_A=16.0 Hz, J_B=12.5 Hz, 2H); 4.07 (d, J=5.0 Hz, 2H); 3.85 (dd, J₁=15.0 Hz, J₂=7.0 Hz, 1H); 3.63 (dd, J₁=J₂=6.5 Hz, 1H); 2.95-2.82 (m, 2H); 2.23 (dd,

$J_1=J_2=7.5$ Hz, 2H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 156.8, 138.3, 136.7, 133.0, 129.5(2C), 128.7(2C), 128.3, 128.1, 126.7, 70.4, 66.9, 63.4, 56.0, 39.0, 37.9. HRMS (ESI) calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_4\text{Na}$ [$\text{M}+\text{Na}$] 378.1681, found 378.1667.

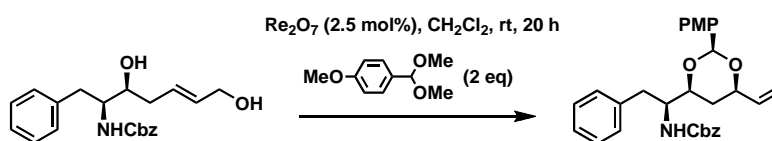


***syn*-6-(Benzyloxycarbonylamino)-5-hydroxy-7-phenylhept-2-enyl acetate.** The typical procedure for cross-metathesis was followed using Hoveyda-Grubbs II catalyst (17 mg, 27.9 μmol), *cis*-1,4-diacetoxy-2-butene (0.480 g, 2.79 mmol) in degassed dichloromethane (4.2 ml). The crude product (*E*-selectivity 10:1) was purified by column chromatography (silica, 30% (350 ml) to 45% (250 ml) to 50% EtOAc – hexanes) delivering the product (57.5 mg, 0.145 mmol, 52%). ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.36-7.18 (m, 10H); 5.86-5.77 (ddd, $J_1=13.5$ Hz, $J_2=J_3=6.5$ Hz, 1H); 5.73-5.67 (ddd, $J_1=12.5$ Hz, $J_2=J_3=6.0$ Hz, 1H); 5.03 (s, 2H); 4.92-4.86 (m, 1H); 4.55-4.54 (d, $J=6.0$ Hz, 2H); 3.96-3.86 (m, 1H); 3.81-3.72 (m, 1H); 2.96 (dd, $J_1=14.0$ Hz, $J_2=4.5$ Hz, 1H); 2.84-2.78 (m, 1H); 2.64-2.58 (m, 1H); 2.39-2.33 (m, 1H); 2.32-2.24 (m, 1H); 2.07 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 171.1, 156.6, 137.9, 136.5, 131.6, 129.5, 128.8, 128.7, 128.3, 128.1, 127.9, 126.8, 72.8, 67.0, 65.0, 56.7, 37.0, 35.5, 21.2. HRMS (ESI) calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_5\text{Na}$ [$\text{M}+\text{Na}$] 378.1681, found 378.1667.



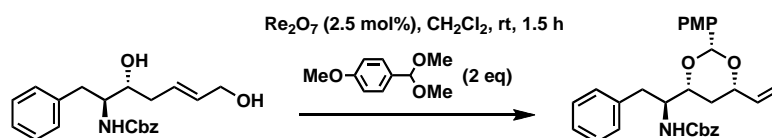
***syn*-Benzyl 3,7-dihydroxy-1-phenylhept-5-en-2-ylcarbamate.** The typical procedure for deacetylation was followed with potassium carbonate (15.1 mg, 0.109 mmol), the substrate (57.5

mg, 0.145 mmol) in methanol (2.9 ml) at rt. The crude product was crystallized in a mixture of EtOAc and hexanes, delivering the product (43.1 mg, 0.121 mmol, 84%). IR (cm⁻¹) 3031.6, 2940.0, 1694.2, 1603.5, 1548.6; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.36-7.17 (m, 10H); 5.79-5.70 (m, 2H); 5.02 (s, 2H); 4.83 (bd, J=8.0 Hz, 1H); 4.13 (bs, 2H); 3.95-3.86 (m, 1H); 3.78-3.71 (m, 1H); 2.96 (dd, J1=14.0 Hz, J2=4.5 Hz, 1H); 2.81 (dd, J1=13.5 Hz, J2=9.5 Hz, 1H); 2.48 (bs, 1H); 2.35 (ddd, J1=13.5 Hz, J2=J3=4.5 Hz, 1H); 2.29-2.23 (m, 1H); 1.60-1.50 (m, 1H). ¹³C NMR (125 MHz, CD₃OD); δ(ppm): 158.6, 140.5, 138.7, 133.2, 130.6, 129.66, 129.54, 129.36, 128.9, 128.6, 127.4, 74.7, 67.2, 63.8, 58.6, 38.0, 37.3. HRMS (ESI) calcd for C₂₁H₂₅NO₄Na [M+Na] 378.1681, found 378.1692.



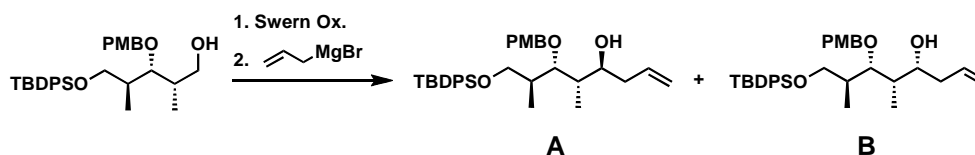
Benzyl 2-(4-methoxyphenyl)-6-vinyl-1,3-dioxan-4-yl)-2-phenylethylcarbamate. The typical procedure was followed: rhenium(VII) oxide (1.2 mg, 2.5 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (0.2 ml). The substrate (35.5 mg, 0.10 mmol) in dichloromethane (0.8 ml total with rinses) was added to the reaction vessel followed by addition of anisaldehyde dimethyl acetal (35 μl, 0.20 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, dichloromethane (to remove anisaldehyde) then 5% ethyl acetate – dichloromethane) delivering the product (33.6 mg, 71 μmol, 71%). IR (cm⁻¹) 3324.7, 3028.7, 2957.3, 1698.0,

1615.1, 1517.7; ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.47 (m, 2H); 7.35-7.18 (m, 10H); 6.92 (m, 2H); 5.92 (ddd, $J_1=16.5$ Hz, $J_2=10.5$ Hz, $J_3=5.5$ Hz, 1H); 5.54 (s, 1H); 5.31 (d, $J=17.0$ Hz, 1H); 5.17 (d, $J=10.5$ Hz, 1H); 5.03 (s, 2H); 4.83 (d, $J=9.5$ Hz, 1H); 4.32-4.26 (m, 1H); 4.08-4.01 (m, 1H); 3.90-3.84 (m, 1H); 3.82 (s, 3H); 3.05 (dd, $J_1=14.0$ Hz, $J_2=3.5$ Hz, 1H); 2.93 (dd, $J_1=14.5$ Hz, $J_2=8.5$ Hz, 1H); 1.74-1.64 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 160.2, 156.1, 137.7, 136.7, 131.1, 129.7, 128.7(2C), 128.3, 128.1, 127.8, 126.7, 116.0, 113.8, 100.8, 77.8, 77.4, 66.8, 55.5, 55.3, 35.7, 33.6. HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_5\text{Na}$ [$\text{M}+\text{Na}$] 496.2100, found 496.2093.



Benzyl 2-(4-methoxyphenyl)-6-vinyl-1,3-dioxan-4-yl)-2-phenylethylcarbamate. The typical procedure was followed: rhenium(VII) oxide (1.2 mg, 2.5 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (0.2 ml). The substrate (35.5 mg, 0.10 mmol) in dichloromethane (0.8 ml total with rinses) was added to the reaction vessel followed by addition of anisaldehyde dimethyl acetal (35 μl , 0.20 mmol). After 1 h 30 min of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, dichloromethane (to remove anisaldehyde) then 5% ethyl acetate – dichloromethane) delivering the product (30.6 mg, 65 μmol , 65%). IR (cm^{-1}) 3430.7, 3331.4, 3028.7, 1717.3, 1648.8, 1516.7, 1248.7; ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 7.47-7.45 (m,

2H); 7.38-7.23 (m, 10H); 6.93-6.91 (m, 2H); 5.87 (ddd, J1=17.0 Hz, J2=10.5 Hz, J3=5.5 Hz, 1H); 5.48 (s, 1H); 5.28 (d, J=17.5 Hz, 1H); 5.21 (d, J=9.5 Hz, 1H); 5.15 (d, J=11.0 Hz, 1H); 5.12 (d, J=13.0 Hz, 1H); 5.06 (d, J=12.5 Hz, 1H); 4.30-4.25 (m, 1H); 3.93 (dd, J1=16.5 Hz, J2=8.0 Hz, 1H); 3.83 (s, 3H); 3.83-3.81 (m, 1H); 3.00-2.92 (m, 2H); 1.76 (dd, J1=24.5 Hz, J2=12.0 Hz, 1H); 1.46 (d, J=13.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 160.2, 156.5, 138.2, 137.6, 136.7, 131.1, 129.6, 128.8, 128.7, 128.3, 128.2, 127.6, 126.7, 115.9, 113.8, 100.6, 77.1, 74.8, 67.0, 55.8, 55.5, 38.5, 33.2. HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_5\text{Na}$ $[\text{M}+\text{Na}]$ 496.2100, found 496.2090.



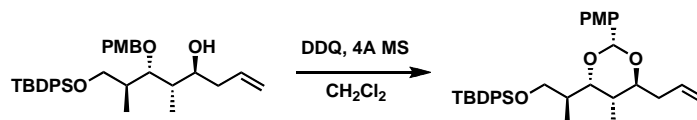
Compounds A and B. Dimethylsulfoxide (0.17 ml, 2.4 mmol) was added to a solution of oxalyl chloride (0.105 ml, 1.18 mmol) in dry dichloromethane (1.9 ml) at $-78\text{ }^{\circ}\text{C}$. After 15 min, a solution of the alcohol¹⁴⁰ (0.300 g, 0.592 mmol) in dichloromethane (4 ml total with rinses) was added. The mixture was stirred for 20 min, and then triethylamine (0.50 ml, 3.55 mmol) was added dropwise. After 15 min the mixture was warmed to $0\text{ }^{\circ}\text{C}$ and stirred for 10 min. The reaction was quenched with 1 M aqueous HCl. The mixture was extracted with ethyl acetate (3x10 ml), and the combined organic layers were washed with water and brine, dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

Allyl magnesium bromide (1M in ether, 0.71 ml, 0.71 mmol), was added to a solution of the crude aldehyde in ether (5.9 ml) at $-78\text{ }^{\circ}\text{C}$. After 30 min of stirring, the reaction was warmed to $-15\text{ }^{\circ}\text{C}$ where it continued to stir for an additional 30 min before being quenched with

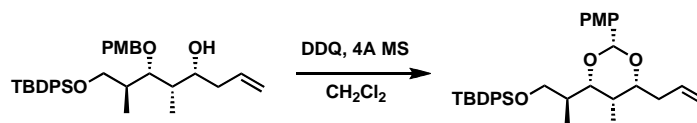
saturated aqueous ammonium chloride. The mixture was extracted with ethyl acetate (3x10 ml). The combined organic layers were washed with water and brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% EtOAc – hexanes) to give product A (88 mg, 0.160 mmol, 27%) and product B (0.175 g, 0.320 mmol, 54% over 2 steps). Data for Product A. $[\alpha]_D^{22} +11.9$ (c 1.0, CH₂Cl₂). IR (cm⁻¹) 3466.4, 3048.9, 2930.3, 1613.2, 1513.9, 1247.7; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.67-7.64 (m, 4H); 7.43-7.40 (m, 2H); 7.38-7.33 (m, 4H); 7.05-7.02 (m, 2H); 6.78-6.75 (m, 2H); 5.89-5.81 (m, 1H); 5.17 (d, J=3.5 Hz, 1H); 5.15 (s, 1H); 4.52 (d, J=10.5 Hz, 1H); 4.39 (d, J=10.5 Hz, 1H); 3.83 (dd, J1=9.0 Hz, J2=1.0 Hz, 1H); 3.80-3.73 (m, 2H); 3.78 (s, 3H); 3.60-3.55 (m, 1H); 2.48-2.42 (m, 1H); 2.23 (d, J=4.0 Hz, 1H); 2.14 (ddd, J1=15.5 Hz, J2=J3=8.0 Hz, 1H); 1.96-1.88 (m, 1H); 1.74-1.68 (m, 1H); 1.09 (s, 9H); 0.96 (d, J=7.0 Hz, 3H); 0.88 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 159.2, 136.00, 135.9, 135.3, 134.1, 134.0, 131.2, 129.8, 129.4, 127.83, 127.78, 118.4, 113.9, 79.7, 73.7, 72.58, 66.2, 55.5, 40.2, 39.8, 38.9, 27.2, 19.5, 14.8, 10.7. HRMS (ESI) calcd for C₃₄H₄₆O₄SiNa [M+Na] 569.3063, found 569.3062. Data for Product B. $[\alpha]_D^{22} +21.7$ (c 1.0, CH₂Cl₂). IR (cm⁻¹) 3466.4, 3048.9, 2930.3, 1613.2, 1513.9, 1247.7; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.67-7.63 (m, 4H); 7.44-7.40 (m, 2H); 7.39-7.33 (m, 4H); 7.03-7.01 (m, 2H); 6.79-6.76 (m, 2H); 5.82 (dddd, J1=18.0 Hz, J2=11.0 Hz, J3=J4=7.5 Hz, 1H); 5.12 (dd, J1=17.5 Hz, J2=1.5 Hz, 1H); 5.09 (dd, J1=12.5 Hz, J2=1.5 Hz, 1H); 4.49 (d, J=10.5 Hz, 1H); 4.43 (d, J=11.0 Hz, 1H); 3.87 (dd, J1=J2=7.0 Hz, 1H); 3.79 (dd, J1=10.0 Hz, J2=5.5 Hz, 1H); 3.78 (s, 3H); 3.73 (dd, J1=9.5 Hz, J2=4.0 Hz, 1H); 3.65 (dd, J1=8.5 Hz, J2=3.0 Hz, 1H); 3.05 (s, 1H); 2.31 (ddd, J1=13.5 Hz, J2=J3=7.0 Hz, 1H); 2.24-2.17 (m, 1H); 2.02-1.97 (m, 1H); 1.81-1.75 (m, 1H); 1.09 (s, 9H); 0.97 (d, J=7.0 Hz, 3H); 0.91 (d, J=7.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 159.4, 136.0, 135.9, 135.7, 133.85, 133.79, 130.3, 129.9, 129.7, 127.9, 127.8,

117.3, 114.0, 85.0, 75.2, 73.8, 65.6, 55.5, 39.9, 38.7, 38.0, 27.2, 19.5, 14.4, 6.7. HRMS (ESI) calcd for C₃₄H₄₆O₄SiNa [M+Na] 569.3063, found 569.3055.

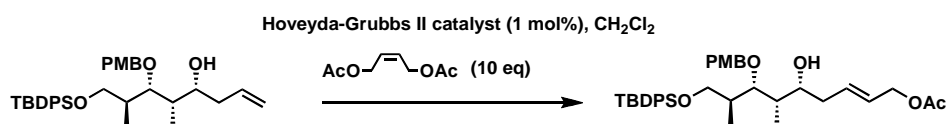
Determination of stereochemistry for Products A and B for the above reaction:



DDQ (9.3 mg, 41.1 μ mol) was added to the substrate (15 mg, 27.4 μ mol) 4A molecular sieves in dichloromethane (0.5 ml) at 0 °C. After 10 min the reaction flask was warmed to rt where it continued to stir for 20 min before being quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 7% EtOAc – hexanes) to give desired product (6 mg, 11 μ mol, 40%). $[\alpha]_D^{22}$ -14.2 (*c* 0.60, CH₂Cl₂). IR (cm⁻¹) 3071.1, 2931.3, 1615.1, 1516.7, 1248.7; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.67-7.62 (m, 4H); 7.42-7.30 (m, 6H); 7.24-7.20 (m, 2H); 6.88-6.85 (m, 2H); 5.86 (dddd, J₁=17.0 Hz, J₂=10.0 Hz, J₃=J₄=7.5 Hz, 1H); 5.68 (s, 1H); 5.14 (dd, J₁=17.0 Hz, J₂=2.0 Hz, 1H); 5.12 (d, J=9.5 Hz, 1H); 4.15 (dd, J₁=10.5 Hz, J₂=2.0 Hz, 1H); 3.99-3.94 (m, 2H); 3.81 (s, 3H); 3.65 (dd, J₁=9.5 Hz, J₂=2.0 Hz, 1H); 2.88-2.82 (m, 1H); 2.57-2.51 (m, 1H); 1.86-1.81 (m, 1H); 1.61 (dddd, J₁=J₂=J₃=7.0 Hz, J₄=1.0 Hz, 1H); 1.20 (d, J=7.0 Hz, 3H); 1.07 (s, 9H); 1.02 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 159.9, 135.8, 135.7, 135.0, 134.1, 132.1, 129.72, 129.65, 127.81, 127.77, 127.57, 117.3, 113.7, 94.9, 79.7, 74.4, 64.9, 55.6, 36.9, 35.4, 31.1, 27.1, 19.7, 13.1, 12.7. HRMS (ESI) calcd for C₃₄H₄₄O₄SiNa [M+Na] 567.2907, found 567.2896.

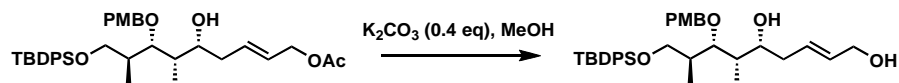


DDQ (8.5 mg, 37.6 μ mol) was added to the substrate (13.7 mg, 25.1 μ mol) 4A molecular sieves in dichloromethane (0.5 ml) at 0 °C. After 10 min the reaction flask was warmed to rt where it continued to stir for 20 min before being quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 7% EtOAc – hexanes) to give desired product (7 mg, 12.8 μ mol, 51%). $[\alpha]_D^{22} +9.8$ (c 0.70, CH₂Cl₂). IR (cm⁻¹) 3071.1, 2930.3, 1616.1, 1517.7, 1248.7; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.67-7.65 (m, 2H); 7.63-7.61 (m, 2H); 7.42-7.38 (m, 1H); 7.36-7.33 (m, 5H); 7.22-7.19 (m, 2H); 6.88-6.85 (m, 2H); 5.91-5.83 (m, 1H); 5.47 (s, 1H); 5.16 (dd, J₁=17.0 Hz, J₂=1.5 Hz, 1H); 5.10 (d, J=10.5 Hz, 1H); 3.96 (dd, J₁=9.5 Hz, J₂=4.0 Hz, 1H); 3.90 (ddd, J₁=J₂=7.0 Hz, J₃=2.0 Hz, 1H); 3.86 (dd, J₁=10.5 Hz, J₂=1.5 Hz, 1H); 3.82 (s, 3H); 3.64 (dd, J₁=9.5 Hz, J₂=2.5 Hz, 1H); 2.52-2.46 (m, 1H); 2.29-2.23 (m, 1H); 1.90-1.86 (m, 1H); 1.64-1.60 (m, 1H); 1.05 (s, 9H); 1.04 (d, J=7.0 Hz, 3H); 0.96 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 159.9, 135.81, 135.76, 134.7, 134.1, 134.0, 131.9, 129.7, 129.6, 127.8, 127.75, 127.6, 117.3, 113.7, 101.4, 81.0, 64.9, 55.6, 37.5, 36.9, 32.1, 27.1, 19.7, 12.6, 5.7. HRMS (ESI) calcd for C₃₄H₄₄O₄SiNa [M+Na] 567.2907, found 567.2894.



(5R,6S,7S,8S,E)-9-(tert-Butyldiphenylsilyloxy)-5-hydroxy-7-(4-methoxybenzyl-oxy)-6,8-dimethylnon-2-enyl acetate. Prepared following the typical procedure for cross-metathesis with

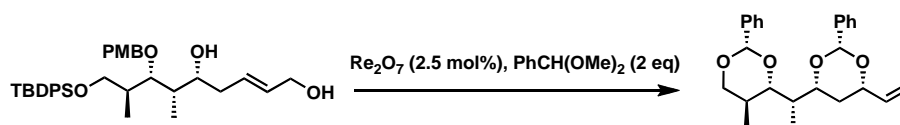
the Hoveyda–Grubbs II catalyst (1.6 mg, 2.51 μ mol) and the substrate (0.137 g, 0.251 mmol). *E*-selectivity >90%. Purified by column chromatography (silica, 20% \rightarrow 30% EtOAc – hexanes) delivering the product (0.138 g, 0.223 mmol, 89%). $[\alpha]_D^{22} +24.8$ (c 1.0, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.67-7.63 (m, 4H); 7.45-7.42 (m, 2H); 7.39-7.35 (m, 4H); 7.02-7.00 (m, 2H); 6.79-6.76 (m, 2H); 5.80 (ddd, J₁=15.0 Hz, J₂=J₃=6.5 Hz, 1H); 5.66 (ddd, J₁=15.5 Hz, J₂=J₃=6.0 Hz, 1H); 4.53 (dd, J₁=6.5 Hz, J₂=1.5 Hz, 2H); 4.68 (d, J=10.5 Hz, 1H); 4.42 (d, J=10.5 Hz, 1H); 3.88 (ddd, J₁=7.5 Hz, J₂=5.5 Hz, J₃=2.0 Hz, 1H); 3.80 (dd, J₁=10.0 Hz, J₂=5.0 Hz, 1H); 3.78 (s, 3H); 3.73 (dd, J₁=10.0 Hz, J₂=4.0 Hz, 1H); 3.64 (dd, J₁=8.0 Hz, J₂=2.5 Hz, 1H); 3.20-3.04 (bs, 1H); 2.33 (ddd, J₁=14.0 Hz, J₂=J₃=7.0 Hz, 1H); 2.21-2.15 (m, 1H); 2.06 (s, 3H); 2.02-1.93 (m, 1H); 1.76-1.72 (m, 1H); 1.09 (s, 9H); 0.97 (d, J=7.0 Hz, 3H); 0.90 (d, J=7.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 171.0, 159.4, 136.0, 135.9, 133.8, 133.7, 133.0, 130.2, 129.9, 129.7, 127.9, 127.8, 126.5, 114.0, 84.9, 75.2, 73.8, 65.6, 65.3, 55.4, 38.6, 38.4, 38.2, 27.2, 21.2, 19.5, 14.4, 6.7. HRMS (ESI) calcd for C₃₇H₅₀O₆SiNa [M+Na] 641.3274, found 641.3255.



(5*R*,6*S*,7*S*,8*S*,*E*)-9-(*tert*-Butyldiphenylsilyloxy)-7-(4-methoxybenzyloxy)-6,8-

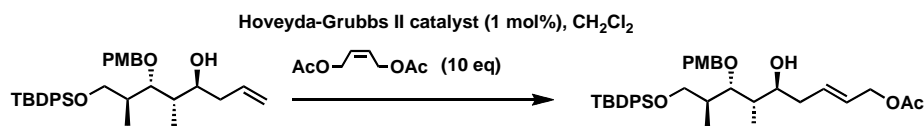
dimethylnon-2-ene-1,5-diol. The typical procedure for deacetylation was followed with 0.138 g (0.223 mmol) of the substrate. Purified by column chromatography (silica, 50% to 60% to 80% EtOAc – hexanes) delivering the product (0.115 g, 0.199 mmol, 89%). $[\alpha]_D^{22} +24.1$ (c 1.0, CH₂Cl₂). IR (cm⁻¹) 3398.0, 3071.1, 2931.3, 1514.8, 1248.7; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.70-7.63 (m, 4H); 7.45-7.42 (m, 2H); 7.39-7.35 (m, 4H); 7.02-7.00 (m, 2H); 6.79-6.76

(m, 2H); 5.75 (dd, J1=15.5 Hz, J2=4.5 Hz, 1H); 5.70 (dd, J1=15.0 Hz, J2=5.0 Hz, 1H); 4.50 (d, J=11.0 Hz, 1H); 4.42 (d, J=10.5 Hz, 1H); 4.11 (bs, 1H); 3.86 (dd, J1=J2=6.0 Hz, 1H); 3.80 (dd, J1=10.5 Hz, J2=5.5 Hz, 1H); 3.78 (s, 3H); 3.73 (dd, J1=10.0 Hz, J2=4.5 Hz, 1H); 3.65 (dd, J1=8.5 Hz, J2=3.0 Hz, 1H); 3.14 (bs, 1H); 2.34-2.28 (m, 1H); 2.19-2.15 (m, 1H); 2.02-1.95 (m, 1H); 1.78-1.71 (m, 1H); 1.44-1.35 (bs, 1H); 1.09 (s, 9H); 0.97 (d, J=7.0 Hz, 3H); 0.90 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 159.4, 135.99, 135.95, 133.82, 133.78, 131.8, 130.3, 129.90, 129.72, 127.94, 127.86, 114.1, 85.0, 75.4, 73.8, 65.6, 63.8, 55.5, 38.6, 38.4, 38.3, 27.2, 19.5, 14.4, 6.7. HRMS (ESI) calcd for C₃₅H₄₈O₅SiNa [M+Na] 599.3169, found 599.3158.



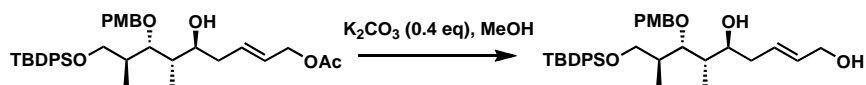
(2*S*,4*S*,5*S*)-5-methyl-2-phenyl-4-((*S*)-1-((2*R*,4*R*,6*S*)-2-phenyl-6-vinyl-1,3-dioxan-4-yl)ethyl)-1,3-dioxane. The typical procedure was followed: rhenium(VII) oxide (1.2 mg, 2.5 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (0.2 ml). The substrate (57.7 mg, 0.10 mmol) in dichloromethane (0.8 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (30 μl, 0.200 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 50% to 80% dichloromethane – hexane) delivering the product (31.1 mg, 79 μmol, 79%). $[\alpha]_D^{22} +39.0$ (*c* 1.0, CH₂Cl₂). IR (cm⁻¹) 3033.5, 2938.0, 1647.9, 1460.8, 1214.0; ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.55-7.53 (m, 2H); 7.49-7.47 (m, 2H);

7.42-7.31 (m, 6H); 5.96 (ddd, J₁=17.0 Hz, J₂=11.0 Hz, J₃=5.5 Hz, 1H); 5.61 (s, 1H); 5.47 (s, 1H); 5.36 (ddd, J₁=17.5 Hz, J₂=J₃=1.5 Hz, 1H); 5.18 (d, J=11.0 Hz, 1H); 4.35-4.33 (m, 1H); 4.14 (dd, J₁=11.0 Hz, J₂=4.5 Hz, 1H); 3.92 (ddd, J₁=11.0 Hz, J₂=8.5 Hz, J₃=2.5 Hz, 1H); 3.65 (dd, J₁=10.5 Hz, J₂=2.0 Hz, 1H); 3.54 (dd, J₁=J₂=11.0 Hz, 1H); 2.18-2.11 (m, 1H); 2.03-1.97 (m, 1H); 1.83 (ddd, J₁=12.5 Hz, J₂=J₃=2.0 Hz, 1H); 1.61-1.55 (m, 1H); 1.19 (d, J=7.0 Hz, 3H); 0.76 (d, J=6.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 139.04, 139.02, 138.2, 128.94, 128.75, 128.44, 128.34, 126.28, 126.25, 115.8, 101.0, 100.6, 81.8, 78.9, 77.4, 73.5, 39.5, 34.6, 30.6, 12.2, 10.1. HRMS (ESI) calcd for C₂₅H₃₀O₄Na [M+Na] 417.2042, found 417.2046.

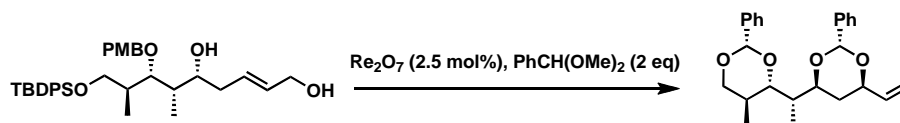


(5S,6S,7S,8S,E)-9-(tert-Butyldiphenylsilyloxy)-5-hydroxy-7-(4-methoxybenzyl-oxy)-6,8-dimethylnon-2-enyl acetate. The typical procedure for cross-metathesis was followed with the Hoveyda-Grubbs II catalyst (1.7 mg, 2.74 μmol) and the substrate (0.150 g, 0.274 mmol). *E*-selectivity >90%. Purified by column chromatography (silica, 20% to 30% EtOAc – hexanes) delivering the product (0.140 g, 0.226 mmol, 83%). $[\alpha]_D^{22} +15.5$ (c 1.0, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃); δ(ppm): 7.66-7.34 (m, 4H); 7.43-7.40 (m, 2H); 7.38-7.33 (m, 4H); 7.05-7.02 (m, 2H); 6.78-6.76 (m, 2H); 5.81 (ddd, J₁=14.0 Hz, J₂=J₃=6.5 Hz, 1H); 5.69 (ddd, J₁=15.5 Hz, J₂=J₃=6.0 Hz, 1H); 4.55 (d, J=6.0 Hz, 2H); 4.51 (d, J=11.5 Hz, 1H); 4.40 (d, J=11.0 Hz, 1H); 3.81 (dd, J₁=9.0 Hz, J₂=1.5 Hz, 1H); 3.78 (s, 3H); 3.78-3.74 (m, 2H); 3.60-3.56 (m, 1H); 2.44-2.39 (m, 1H); 2.31 (d, J=4.5 Hz, 1H); 2.19-2.13 (m, 1H); 2.06 (s, 3H); 1.95-1.90 (m, 1H); 1.73-1.68 (m, 1H); 1.09 (s, 9H); 0.96 (d, J=7.0 Hz, 3H); 0.88 (d, J=7.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 171.0, 159.2, 136.0, 135.9, 134.0, 133.9, 132.4, 131.1, 129.8, 129.4, 127.81,

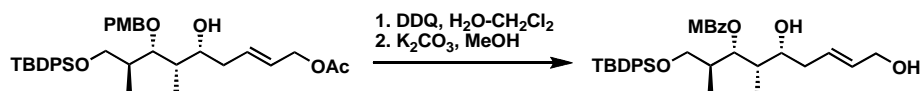
127.76, 127.46, 113.8, 79.8, 73.5, 72.9, 66.1, 65.1, 55.4, 39.8, 38.8, 38.6, 27.2, 21.2, 19.5, 14.8, 11.0. HRMS (ESI) calcd for C₃₇H₅₀O₆SiNa [M+Na] 641.3274, found 641.3262.



(5*S*,6*S*,7*S*,8*S*,*E*)-9-(*tert*-butyldiphenylsilyloxy)-7-(4-methoxybenzyloxy)-6,8-dimethylnon-2-ene-1,5-diol. The typical procedure for deacetylation was followed with 0.140 g (0.226 mmol) of the substrate. Purified by column chromatography (silica, 50% to 60% to 80% EtOAc – hexanes) delivering the product (0.110 g, 0.191 mmol, 84%). $[\alpha]_D^{22} +18.6$ (*c* 1.0, CH₂Cl₂). IR (cm⁻¹) 3366.1, 3070.1, 2930.3, 1513.9, 1247.7; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.68-7.63 (m, 4H); 7.44-7.40 (m, 2H); 7.40-7.33 (m, 4H); 7.04-7.02 (m, 2H); 6.78-6.76 (m, 2H); 5.772 (dd, *J*₁=15.5 Hz, *J*₂=5.0 Hz, 1H); 5.72 (dd, *J*₁=15.0 Hz, *J*₂=5.5 Hz, 1H); 4.50 (d, *J*=10.5 Hz, 1H); 4.40 (d, *J*=11.0 Hz, 1H); 4.15-4.11 (m, 2H); 3.82 (d, *J*=9.5 Hz, 1H); 3.78 (s, 3H); 3.78-3.74 (m, 1H); 3.59-3.53 (m, 1H); 2.45-2.39 (m, 1H); 2.39-2.28 (m, 1H); 2.17 (s, 1H); 2.17-2.11 (m, 1H); 1.97-1.88 (m, 1H); 1.75-1.67 (m, 1H); 1.09 (s, 9H); 0.966 (d, *J*=7.0 Hz, 3H); 0.886 (d, *J*=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 159.9, 135.98, 135.94, 134.03, 133.98, 132.7, 131.1, 129.76, 129.44, 129.10, 127.83, 127.78, 113.9, 79.8, 73.6, 73.0, 66.1, 63.6, 55.4, 39.9, 38.8, 38.5, 27.2, 19.5, 14.8, 11.0. HRMS (ESI) calcd for C₃₅H₄₈O₅SiNa [M+Na] 599.3169, found 599.3147.

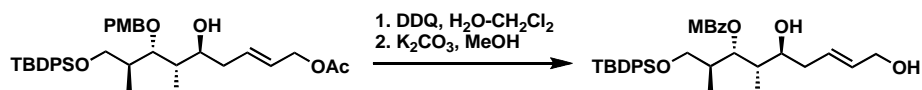


(2*S*,4*S*,5*S*)-5-Methyl-2-phenyl-4-((*S*)-1-((2*R*,4*S*,6*R*)-2-phenyl-6-vinyl-1,3-dioxan-4-yl)ethyl)-1,3-dioxane. The typical procedure was followed: rhenium(VII) oxide (1.2 mg, 2.5 μ mol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (0.2 ml). The substrate (57.7 mg, 0.10 mmol) in dichloromethane (0.8 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (30 μ l, 0.200 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 50% to 80% dichloromethane – hexane) delivering the product (33.1 mg, 84 μ mol, 84%). $[\alpha]_D^{22} +76.8$ (*c* 1.0, CH₂Cl₂). IR (cm⁻¹) 3034.4, 2928.4, 1647.9, 1585.2, 1274.7; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.54-7.50 (m, 2H); 7.50-7.47 (m, 2H); 7.43-7.33 (m, 6H); 5.96 (ddd, J₁=17.0 Hz, J₂=10.5 Hz, J₃=5.5 Hz, 1H); 5.60 (s, 1H); 5.52 (s, 1H); 5.35 (ddd, J₁=17.5 Hz, J₂=J₃=1.5 Hz, 1H); 5.17 (ddd, J₁=10.5 Hz, J₂=J₃=1.5 Hz, 1H); 4.38-4.35 (m, 1H); 4.14 (dd, J₁=11.0 Hz, J₂=4.5 Hz, 1H); 4.00-3.96 (m, 2H); 3.56 (dd, J₁=J₂=11.0 Hz, 1H); 2.13-2.06 (m, 1H); 2.01-1.95 (m, 1H); 1.84 (ddd, J₁=13.0 Hz, J₂=J₃=2.0 Hz, 1H); 1.53-1.46 (m, 1H); 1.00 (d, J=7.5 Hz, 3H); 0.75 (d, J=6.5 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 139.3, 139.0, 138.2, 128.83, 128.75, 128.38, 128.35, 126.28, 126.25, 115.7, 101.2, 100.4, 81.0, 77.6, 76.9, 73.5, 39.2, 35.4, 30.4, 12.2, 8.7. HRMS (ESI) calcd for C₂₅H₃₀O₄Na [M+Na] 417.2042, found 417.2050.



(2*S*,3*S*,4*S*,5*R*,*E*)-1-(*tert*-Butyldiphenylsilyloxy)-5,9-dihydroxy-2,4-dimethylnon-7-en-3-yl benzoate. DDQ (0.180 g, 0.795 mmol) was added to a solution of the substrate (0.164 g, 0.265 mmol) in dichloromethane (5.3 ml) and water (4.8 μ l) at rt. After stirring for 4 h the reaction mixture was quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

Potassium carbonate (14.7 mg, 0.106 mmol) was added to a solution of the crude substrate in methanol (2.7 ml) at 0 C. After 10 min the reaction was warmed to rt and continued to stir for 1 h. Dilute with water and ethyl acetate. The mixture was extracted with ethyl acetate (4x30 ml), and the organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% \rightarrow 40% \rightarrow 60% EtOAc – hexanes) delivering the product (83.4 mg, 0.141 mmol, 53% over 2 steps). $[\alpha]_D^{22}$ -4.9 (*c* 1.0, CH₂Cl₂). IR (cm⁻¹) 3388.3, 3048.9, 2931.3, 1709.6, 1605.5, 1510.0, 1257.4; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.91-7.89 (m, 2H); 7.64-7.62 (m, 2H); 7.57-7.55 (m, 2H); 7.41-7.31 (m, 4H); 7.26-7.23 (m, 2H); 6.09-6.87 (m, 2H); 5.73 (ddd, J₁=15.0 Hz, J₂=J₃=10.0 Hz, 1H); 5.68 (ddd, J₁=16.0 Hz, J₂=J₃=9.5 Hz, 1H); 5.23 (dd, J₁=8.0 Hz, J₂=4.0 Hz, 1H); 4.08 (d, J=4.5 Hz, 2H); 3.87 (s, 3H); 3.73-3.68 (s, 1H); 3.64 (dd, J₁=10.0 Hz, J₂=4.5 Hz, 1H); 3.57 (dd, J₁=10.0 Hz, J₂=6.0 Hz, 1H); 2.33 (ddd, J₁=14.5 Hz, J₂=J₃=5.5 Hz, 1H); 2.27-2.21 (m, 2H); 2.19-2.12 (m, 1H); 2.01-1.95 (m, 1H); 1.46-1.32 (m, 1H); 1.04 (d, J=7.0 Hz, 3H); 1.02 (s, 9H); 0.98 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 166.6, 163.6, 135.80, 135.76, 133.8, 133.6, 132.5, 131.9, 129.76, 129.69, 129.3, 127.8, 127.7, 122.8, 113.8, 76.9, 73.2, 65.3, 63.7, 55.7, 39.6, 38.5, 38.0, 27.0, 19.4, 14.6, 8.6. HRMS (ESI) calcd for C₃₅H₄₆O₆SiNa [M+Na] 613.2961, found 613.2939.

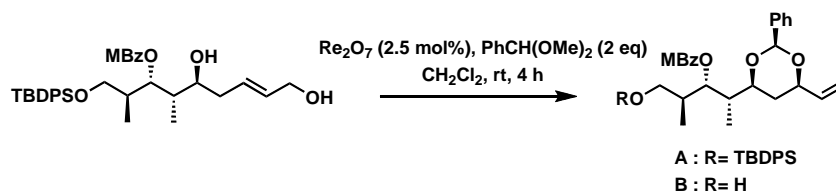


(2*S*,3*S*,4*S*,5*S*,*E*)-1-(*tert*-Butyldiphenylsilyloxy)-5,9-dihydroxy-2,4-dimethylnon-7-en-3-yl benzoate. DDQ (86.5 mg, 0.381 mmol) was added to a solution of the substrate (78.5 mg, 0.127 mmol) in dichloromethane (2.5 ml) and water (4.8 μ l) at rt. After stirring for 5 h the reaction mixture was quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

Potassium carbonate (7.1 mg, 51 μ mol) was added to a solution of the crude substrate in methanol (1.3 ml) at 0 C. After 10 min the reaction was warmed to rt and continued to stir for 1 h 20 min. Dilute with water and ethyl acetate. The mixture was extracted with ethyl acetate (4x30 ml), and the organic layers were washed with brine, dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 20% \rightarrow 40% \rightarrow 60% EtOAc – hexanes) delivering the product (44.7 mg, 75.7 μ mol, 60% over 2 steps). $[\alpha]_D^{22}$ -11.1 (*c* 1.0, CH₂Cl₂). IR (cm⁻¹) 3428.8, 3048.9, 2930.3, 1687.4, 1605.5, 1511.0, 1258.3; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.92-7.89 (m, 2H); 7.61-7.59 (m, 2H); 7.47-7.46 (m, 2H); 7.39-7.36 (m, 1H); 7.32-7.22 (m, 3H); 7.13-7.10 (m, 2H); 6.91-6.88 (m, 2H); 5.85 (ddd, *J*₁=15.5 Hz, *J*₂=*J*₃=7.0 Hz, 1H); 5.71 (ddd, *J*₁=15.0 Hz, *J*₂=*J*₃=5.5 Hz, 1H); 5.66 (d, *J*=10.0 Hz, 1H); 4.33 (d, *J*=3.5 Hz, 1H); 4.13-4.08 (m, 2H); 3.89 (s, 3H); 3.61 (dd, *J*₁=9.5 Hz, *J*₂=5.0 Hz, 1H); 3.55 (dd, *J*₁=10.0 Hz, *J*₂=2.5 Hz, 1H); 3.22-3.14 (m, 1H); 2.45-2.38 (m, 1H); 2.20-2.06 (m, 2H); 1.84-1.77 (m, 1H); 1.83 (d, *J*=7.0 Hz, 3H); 1.0 (s, 9H); 0.89 (d, *J*=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 167.6, 163.8, 135.8, 135.7, 133.7, 133.5, 132.1, 131.4, 130.0, 129.7, 129.6,

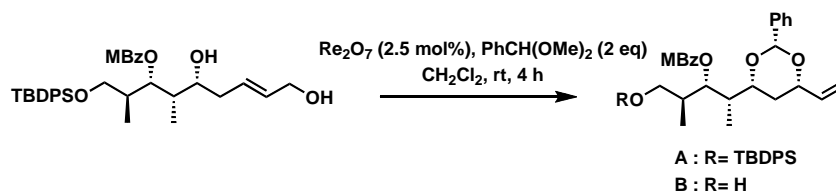
127.7, 127.6, 122.2, 113.9, 74.7, 71.6, 65.5, 63.9, 55.7, 40.5, 37.5, 37.1, 27.0, 19.4, 14.4, 9.7.

HRMS (ESI) calcd for C₃₅H₄₆O₆SiNa [M+Na] 613.2961, found 613.2964.



(2S,3S,4S)-1-Hydroxy-2-methyl-4-((2S,4S,6R)-2-phenyl-6-vinyl-1,3-dioxan-4-yl)pentan-3-yl 4-methoxybenzoate. According to the typical procedure, rhenium(VII) oxide (0.8 mg, 1.7 μ mol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (0.1 ml). The substrate (39 mg, 66 μ mol) in dichloromethane (0.6 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (20 μ l, 0.13 mmol). After 4 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% to 20% to 30% EtOAc – hexane) delivering compound **A** (11.0 mg, 16.2 μ mol, 25%) and compound **B** (16.3 mg, 38.4 μ mol, 58%). Data for compound A: $[\alpha]_D^{22} +48.3$ (*c* 0.82, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.94-7.91 (m, 2H); 7.73-7.71 (m, 1H); 7.65-7.61 (m, 4H); 7.57-7.55 (m, 2H); 7.42-7.27 (m, 6H); 7.22-7.15 (m, 2H); 6.92-6.89 (m, 2H); 5.93 (ddd, J₁=17.5 Hz, J₂=10.5 Hz, J₃=5.5 Hz, 1H); 5.67 (dd, J₁=9.5 Hz, J₂=2.0 Hz, 1H); 5.53 (s, 1H); 5.33 (ddd, J₁=17.5 Hz, J₂=J₃=1.0 Hz, 1H); 5.16 (ddd, J₁=11.0 Hz, J₂=J₃=1.5 Hz, 1H); 4.29-4.26 (m, 1H); 3.88 (s, 3H); 3.67 (ddd, J₁=11.0 Hz, J₂=9.0 Hz, J₃=2.0 Hz, 1H); 3.63-3.60 (m, 2H); 2.14-2.02 (m, 2H); 1.68 (ddd, J₁=13.0 Hz, J₂=J₃=2.0 Hz, 1H); 1.51-1.44 (m, 1H);

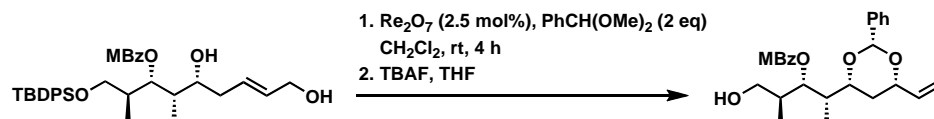
1.07 (d, $J=7.0$ Hz, 3H); 1.02 (s, 9H); 0.972 (d, $J=7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 165.6, 163.4, 138.9, 138.2, 135.9, 135.8, 133.9, 133.8, 131.8, 129.64, 129.58, 128.5, 128.2, 127.73, 127.67, 126.4, 123.2, 115.5, 113.8, 100.2, 77.6, 73.6, 65.6, 55.7, 39.9, 38.2, 34.9, 29.9, 27.0, 19.4, 14.6, 8.9. HRMS (ESI) calcd for $\text{C}_{42}\text{H}_{50}\text{O}_6\text{SiNa}$ $[\text{M}+\text{Na}]$ 701.3274, found 701.3261. Data for **compound B**: $[\alpha]_{\text{D}}^{22} +112.2$ (c 1.00, CH_2Cl_2). ^1H NMR (500 MHz, CDCl_3); $\delta(\text{ppm})$: 8.03-7.98 (m, 2H); 7.52-7.51 (m, 2H); 7.37-7.28 (m, 3H); 6.95-6.91 (m, 2H); 5.93 (ddd, $J_1=17.0$ Hz, $J_2=10.5$ Hz, $J_3=5.5$ Hz, 1H); 5.58 (dd, $J_1=10.0$ Hz, $J_2=1.5$ Hz, 1H); 5.35 (s, 1H); 5.33 (ddd, $J_1=17.0$ Hz, $J_2=J_3=1.5$ Hz, 1H) 5.17 (ddd, $J_1=10.5$ Hz, $J_2=J_3=1.5$ Hz, 1H); 4.28-4.25 (m, 1H); 3.87 (s, 3H); 3.67 (ddd, $J_1=11.0$ Hz, $J_2=9.0$, $J_3=2.0$ Hz, 1H); 3.60-3.56 (m, 1H); 3.49-3.44 (m, 1H); 2.90-2.82 (bs, 1H); 2.10-2.04 (m, 1H); 1.98-1.91 (m, 1H); 1.79 (ddd, $J_1=13.0$ Hz, $J_2=J_3=2.5$ Hz, 1H); 1.53-1.46 (m, 1H); 1.09 (d, $J=7.0$ Hz, 3H); 1.06 (d, $J=7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3); $\delta(\text{ppm})$: 167.3, 163.9, 138.5, 138.0, 132.0, 128.7, 128.3, 126.2, 122.4, 115.7, 114.0, 100.2, 77.9, 77.3, 73.3, 64.2, 55.7, 39.4, 37.3, 35.3, 14.0, 9.0. HRMS (ESI) calcd for $\text{C}_{26}\text{H}_{32}\text{O}_6\text{SiNa}$ $[\text{M}+\text{Na}]$ 463.2097, found 463.2090.



(2*S*,3*S*,4*S*)-1-Hydroxy-2-methyl-4-((2*R*,4*R*,6*S*)-2-phenyl-6-vinyl-1,3-dioxan-4-yl)pentan-3-yl 4-methoxybenzoate. In accord with the typical procedure, rhenium(VII) oxide (0.9 mg, 1.9 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (0.1 ml). The substrate (44 mg, 75 μmol) in dichloromethane (0.7 ml total with rinses) was added to the reaction vessel followed by

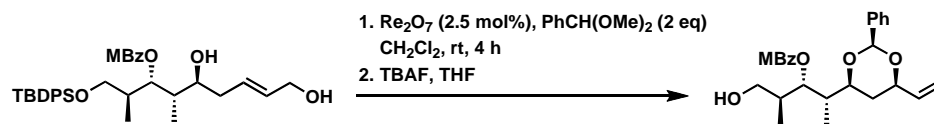
addition of benzaldehyde dimethyl acetal (22 μ l, 0.15 mmol). After 4 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% \rightarrow 30% EtOAc – hexane) delivering product **A** (24.2 mg, 35.6 μ mol, 48%) and product **B** (12.5 mg, 28.4 μ mol, 38%). Data for compound A: $[\alpha]_D^{22} +0.2$ (c 1.00, CH₂Cl₂). IR (cm⁻¹) 3048.9, 2930.3, 1709.6, 1605.5, 1510.0, 1257.4; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.87-7.84 (m, 2H); 7.26-7.61 (m, 2H); 7.56-7.55 (m, 2H); 7.42-7.21 (m, 11H); 6.87-6.84 (m, 2H); 5.94 (ddd, J₁=17.5 Hz, J₂=10.5, J₃=5.5 Hz, 1H); 5.47 (s, 1H); 5.35 (d, J=17.5 Hz, 1H); 5.31 (dd, J₁=9.0 Hz, J₂=3.0 Hz, 1H); 5.16 (d, J=10.5 Hz, 1H); 4.32-4.29 (m, 1H); 3.87 (s, 3H); 3.78 (ddd, J₁=11.0 Hz, J₂=7.0 Hz, J₃=2.0 Hz, 1H); 3.62 (dd, J₁=10.5 Hz, J₂=4.0 Hz, 1H); 3.56 (dd, J₁=10.5 Hz, J₂=6.5 Hz, 1H); 2.17 (m, 1H); 2.05-1.99 (m, 2H); 1.57-1.50 (m, 1H); 1.13 (d, J=6.5 Hz, 3H); 1.06, (d, J=6.5 Hz, 3H); 1.02 (s, 9H). ¹³C NMR (125 MHz, CDCl₃); δ (ppm): 166.0, 163.4, 138.9, 138.1, 135.8, 133.9, 133.7, 131.9, 129.71, 129.66, 128.5, 128.1, 127.8, 127.7, 126.3, 123.0, 115.5, 113.7, 100.5, 78.6, 77.2, 74.9, 65.4, 55.7, 40.3, 38.0, 35.1, 27.0, 19.4, 14.7, 9.3. HRMS (ESI) calcd for C₄₂H₅₀O₆SiNa [M+Na] 701.3274, found 701.3267. Data for compound B: $[\alpha]_D^{22} +11.1$ (c 1.00, CH₂Cl₂). IR (cm⁻¹) 3493.4, 3035.4, 2925.5, 1708.6, 1605.5, 1511.0, 1258.3; ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.99-7.96 (m, 2H); 7.44-7.42 (m, 2H); 7.31-7.27 (m, 3H); 6.92-6.89 (m, 2H); 5.91 (ddd, J₁=17.0 Hz, J₂=10.5 Hz, J₃=5.0 Hz, 1H); 5.49 (s, 1H); 5.32 (dd, J₁=17.5 Hz, J₂=J₃=1.5 Hz, 1H); 5.22 (dd, J₁=10.5 Hz, J₂=2.5 Hz, 1H); 5.16 (ddd, J₁=10.5 Hz, J₂=J₃=1.5 Hz, 1H); 4.26-4.22 (m, 1H); 3.87 (s, 3H); 3.72 (ddd, J₁=11.0 Hz, J₂=7.5 Hz, J₃=2.0 Hz, 1H); 3.56 (dd, J₁=11.5 Hz, J₂=2.5 Hz, 1H); 3.48 (bd, J=11.5 Hz, 1H); 2.58-2.48 (bs, 1H); 2.09-1.96 (m, 2H); 1.82 (ddd, J₁=13.0 Hz, J₂=J₃=2.5 Hz, 1H); 1.58-1.51 (m,

1H); 1.25 (d, J=7.0 Hz, 3H); 1.07 (d, J=7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃); δ(ppm): 167.4, 164.0, 138.8, 137.8, 132.2, 128.7, 128.2, 126.3, 122.1, 115.8, 114.0, 100.7, 79.1, 77.1, 74.5, 64.0, 55.7, 39.9, 37.4, 35.0, 14.2, 9.4. HRMS (ESI) calcd for C₂₆H₃₂O₆Na [M+Na] 463.2097, found 463.2090.



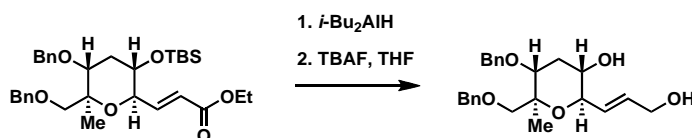
(2*S*,3*S*,4*S*)-1-Hydroxy-2-methyl-4-((2*R*,4*R*,6*S*)-2-phenyl-6-vinyl-1,3-dioxan-4-yl)pentan-3-yl 4-methoxybenzoate (procedure for two steps). According to the typical procedure, rhenium(VII) oxide (0.8 mg, 1.7 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). Dichloromethane (0.1 ml) was added to the flask. The substrate (34 mg, 58 μmol) in dichloromethane (0.7 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (18 μl, 0.12 mmol). After 4 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

Tetra-*n*-butylammonium fluoride (1M in THF, 0.18 ml, 0.18 mmol) was added to a solution of the crude residue in THF (0.8 ml). After 1 h 30 min the reaction was quenched with saturated aqueous ammonium chloride. The mixture was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% to 20% to 30% EtOAc – hexane) delivering the product (19 mg, 44 μmol, 76% over two steps).



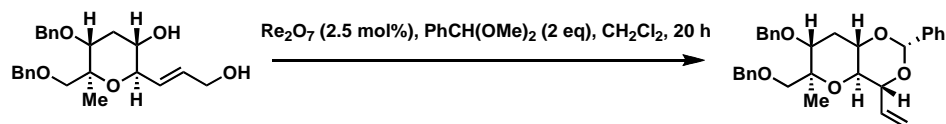
(2*S*,3*S*,4*S*)-1-Hydroxy-2-methyl-4-((2*S*,4*S*,6*R*)-2-phenyl-6-vinyl-1,3-dioxan-4-yl)pentan-3-yl 4-methoxybenzoate (procedure for two steps). According to the typical procedure, rhenium(VII) oxide (0.4 mg, 0.9 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). Dichloromethane (0.1 ml) was added to the flask. The substrate (16 mg, 27 μmol) in dichloromethane (0.4 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (10 μl , 54 μmol). After 4 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was submitted to the next reaction without further purification.

Tetra-*n*-butylammonium fluoride (1M in THF, 0.10 ml, 0.10 mmol) was added to a solution of the crude residue in THF (0.5 ml). After 1 h the reaction was quenched with saturated aqueous ammonium chloride. The mixture was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% to 20% to 30% EtOAc – hexane) delivering the product (10 mg, 23 μmol , 84% over two steps).



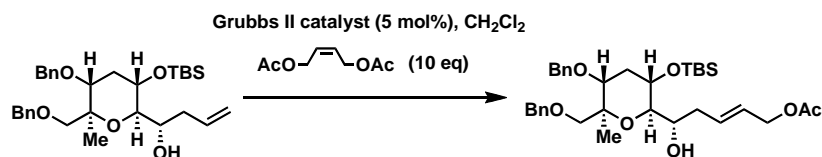
(2R,3S,5R,6S)-5-(Benzyloxy)-6-(benzyloxymethyl)-2-((E)-3-hydroxyprop-1-enyl)-6-methyltetrahydro-2H-pyran-3-ol. Diisobutylaluminum hydride (1 M in toluene, 1.7 ml, 1.7 mmol) was added to a solution of the substrate¹⁴¹ (0.473 g, 0.788 mmol) in dichloromethane (8 ml) at -78 °C. After stirring at the same temperature for 1 h, *i*-PrOH, H₂O, SiO₂, Celite and dichloromethane were added and the mixture was warmed to rt. The mixture was stirred at rt for 1 h. MgSO₄ was added. The mixture was filtered through a pad of Celite and the filtrate was concentrated *in vacuo*. The residue was passed through a short column (silica, *n*-hexane:EtOAc = 3:1).

Tetra-*n*-butylammonium fluoride (1M in THF, 1.18 ml, 1.18 mmol) was added to a solution of the crude substrate at room temperature. The solution was stirred at room temperature for 1 h. Water was added and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, *n*-hexane:EtOAc = 3:1 to 2:1) to give the diol (0.307 g, 0.770 mmol, 98% over 2 steps). $[\alpha]_D^{22}$ -9.0 (*c* 1.0, CH₂Cl₂). IR (cm⁻¹) 3367.2, 2987.2, 2940.9, 1605.5, 1496.5, 1455, 1370.2, 1207.2, 1089.6, 904.5, 736.7, 698.1; ¹H NMR (500 MHz, CDCl₃) δ 7.31–7.22 (m, 10H), 6.00 (ddd, *J* = 16.0, 5.0, 5.0 Hz, 1H), 5.75 (dd, *J* = 16.0, 7.5 Hz, 1H), 4.63 (d, *J* = 12.5 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.52 (d, *J* = 12.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 4.19 (d, *J* = 4.5 Hz, 2H), 3.81 (m, 1H), 3.78 (dd, *J* = 12.0, 5.0 Hz, 1H), 3.55 (d, *J* = 10.5 Hz, 1H), 3.45 (d, *J* = 10.5 Hz, 1H), 3.35 (ddd, *J* = 11.5, 9.5, 5.0 Hz, 1H), 2.39 (ddd, *J* = 12.0, 4.5, 4.5 Hz, 1H), 1.85 (bs, 1H), 1.63 (ddd, *J* = 12.0, 12.0, 12.0 Hz, 1H), 1.20 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.7 (2C), 134.0, 129.7, 128.51 (2C), 128.50 (2C), 127.9 (2C), 127.73 (2C), 127.71 (2C), 77.6, 76.1, 74.7, 73.84, 73.79, 71.5, 69.5, 63.0, 32.9, 13.8; HRMS (ESI) calcd for C₂₄H₃₀O₅Na [(M + Na⁺)] 421.1991, found 421.1982.

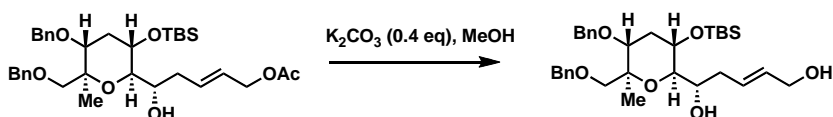


(2*S*,4*R*,4*aS*,6*S*,7*R*,8*aS*)-7-(Benzyloxy)-6-(benzyloxymethyl)-6-methyl-2-phenyl-4-vinylhexahydropyrano[3,2-*d*][1,3]dioxine. Following the typical procedure, rhenium(VII) oxide (4.0 mg, 8.16 μ mol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3). To the flask was added dichloromethane (1.25 ml). The substrate (0.130 g, 0.326 mmol) in dichloromethane (2.0 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (0.10 ml, 0.65 mmol). The reaction vessel was sealed and heated at 40 $^{\circ}$ C. After 20 h the reaction was allowed to cool to rt and saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min. The aqueous layer was extracted with dichloromethane (3x10 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% EtOAc – hexane) delivering the product (0.128 g, 0.263 mmol, 81%). $[\alpha]_D^{22} +5.2$ (*c* 1.0, CH_2Cl_2). IR (cm^{-1}) 3088, 3063.4, 3030.6, 2987.2, 2944.8, 2859, 1496.5, 1454.1, 1365.4, 1292.1, 1207.2, 1097.3, 1027.9, 926.6; ^1H NMR (500 MHz, CDCl_3) δ 7.54–7.52 (m, 2H), 7.39–7.24 (m, 13H), 6.02 (ddd, J = 17.5, 10.5, 5.5 Hz, 1H), 5.66 (s, 1H), 5.47 (ddd, J = 17.5, 1.5, 1.5 Hz, 1H), 5.27 (ddd, J = 10.5, 1.5, 1.5 Hz, 1H), 4.64–4.56 (m, 3H), 4.44 (d, J = 11.5 Hz, 1H), 4.19 (dd, J = 9.0, 5.0 Hz, 1H), 3.88 (ddd, J = 11.5, 4.5 Hz, 1H), 3.57 (m, 1H), 3.57 (d, J = 10.5 Hz, 1H), 3.48 (d, J = 10.5 Hz, 1H), 3.31 (dd, J = 9.0, 9.0 Hz, 1H), 2.46 (ddd, J = 11.5, 4.0, 4.0 Hz, 1H), 1.78 (ddd, J = 11.5, 11.5, 11.5 Hz, 1H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.8, 138.5, 137.8, 134.7, 129.1, 128.5 (3C), 128.4 (2C), 127.74 (3C), 127.67 (2C), 127.6 (2C), 126.4 (2C), 117.2, 101.2, 79.7, 79.0, 76.6, 74.4, 74.1,

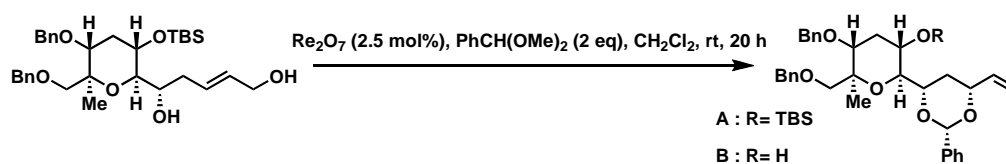
73.7, 71.43, 71.41, 30.6, 14.2; HRMS (ESI) calcd for C₃₁H₃₄O₅Na [M+Na] 509.2304, found 509.2296.



(*S,E*)-5-((2*R*,3*S*,5*R*,6*S*)-5-(Benzyloxy)-6-(benzyloxymethyl)-3-(*tert*-butyldimethylsilyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)-5-hydroxypent-2-enyl acetate. Prepared according to the typical procedure for cross-metathesis using Grubbs II catalyst (6.8 mg, 8.1 μ mol) and 85 mg (0.161 mmol) of the substrate. *E*-selectivity >90%. Purified by column chromatography (silica, 25% EtOAc - hexanes) delivering the product (92 mg, 0.154 mmol, 96%). $[\alpha]_D^{22} +13$ (*c* 1.0, CH₂Cl₂). ¹H NMR (500 MHz, CDCl₃); δ (ppm): 7.35-7.26 (m, 10H); 5.78 (ddd, J₁=14.5 Hz, J₂=7.5 Hz, J₃=6.5 Hz, 1H); 5.64 (ddd, J₁=15.0 Hz, J₂=J₃=6.5 Hz, 1H); 4.54 (d, J=12.0 Hz, 1H); 4.56-4.50 (m, 3H); 4.45 (d, J=11.5 Hz, 1H); 3.78 (bs, 1H); 3.70-3.65 (m, 2H); 3.54 (d, J=10.5 Hz, 1H); 3.42 (d, J=10.0 Hz, 1H); 3.18 (dd, J₁=9.5 Hz, J₂=1.0 Hz, 1H); 2.41-2.34 (m, 1H); 2.31-2.25 (m, 1H); 2.20-2.16 (m, 2H); 2.05 (s, 3H); 1.82 (bs, 1H); 1.57 (dd, J₁=24.0 Hz, J₂=11.5 Hz, 1H); 1.13 (s, 3H); 0.87 (s, 9H); 0.08 (s, 3H); 0.06 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 171.0, 138.8, 138.6, 132.7, 128.58, 128.56, 128.14, 127.79, 127.78, 127.77, 126.5, 77.3, 75.2, 74.8, 73.60, 73.55, 71.7, 68.5, 66.3, 65.3, 37.9, 34.6, 26.0 (3C), 21.2, 18.1, 13.8, -4.0, -4.6. HRMS (ESI) calcd for C₃₄H₅₀O₇SiNa [M+Na] 621.3224, found 621.3217.



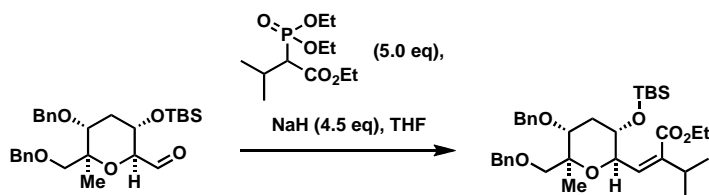
(*S,E*)-5-((2*R*,3*S*,5*R*,6*S*)-5-(Benzyloxy)-6-(benzyloxymethyl)-3-(*tert*-butyldimethylsilyloxy)-6-methyltetrahydro-2*H*-pyran-2-yl)pent-2-ene-1,5-diol. Prepared according to the typical procedure for deacetylation from 92 mg (0.154 mmol) of the substrate. Purified by column chromatography (silica, 65% to 80% EtOAc – hexanes) delivering the product (80 mg, 0.144 mmol, 93%). $[\alpha]_D^{22}$ –6.7 (*c* 1.0, CH₂Cl₂); IR (cm^{–1}) 3426.9, 3064.2, 3030.6, 2926.5, 2855.1, 1496.5, 1455, 1362.5, 1252.5, 1208.2, 1088.6, 864, 837; ¹H NMR (500 MHz, CDCl₃) δ 7.33–7.24 (m, 10H), 5.70 (m, 2H), 4.56–4.50 (m, 3H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.08 (d, *J* = 3.0 Hz, 2H), 3.77 (dd, *J* = 7.0, 7.0 Hz, 1H), 3.67 (ddd, *J* = 10.5, 4.5, 4.5 Hz, 1H), 3.62 (dd, *J* = 12.0, 5.0 Hz, 1H), 3.51 (d, *J* = 11.0 Hz, 1H), 3.42 (d, *J* = 11.0 Hz, 1H), 3.19 (d, *J* = 9.0 Hz, 1H), 2.35 (m, 1H), 2.27 (m, 1H), 2.17 (ddd, *J* = 12.0, 5.0, 5.0 Hz, 1H), 1.60 (bs, 1H), 1.56 (ddd, *J* = 11.5, 11.5, 11.5 Hz, 1H), 1.14 (s, 3H) 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 138.8, 138.6, 131.7, 129.4, 128.6 (2C), 128.5 (2C), 127.82 (2C), 127.81 (2C), 127.79 (2C), 77.3, 75.4, 74.9, 73.7, 73.6, 71.7, 68.6, 66.3, 63.9, 38.0, 34.6, 26.0 (3C), 18.2, 13.8, –4.0, –4.6; HRMS (ESI) calcd for C₃₂H₄₈O₆SiNa [M+Na] 579.3118, found 579.3103.



Compounds A and B. The typical procedure was followed: rhenium(VII) oxide (1.7 mg, 3.6 μmol) was quickly weighed out into a flame-dried flask. The flask was evacuated and backfilled with argon (x3), and dichloromethane (0.4 ml) was added. The substrate (80 mg, 0.144 mmol) in dichloromethane (1.0 ml total with rinses) was added to the reaction vessel followed by addition of benzaldehyde dimethyl acetal (45 μl, 0.288 mmol). After 20 h of stirring at rt, saturated aqueous sodium bicarbonate was added and the biphasic mixture stirred vigorously for 10 min.

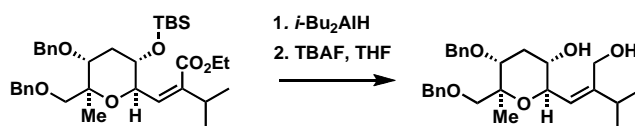
The aqueous layer was extracted with dichloromethane (3x5 ml). The combined organic layers were dried with sodium sulfate, concentrated, and the residue was purified by column chromatography (silica, 10% to 20% to 50% EtOAc – hexanes) delivering the product **A** (11.8 mg, 18.3 μ mol, 13%) and product **B** (52.6 mg, 99.1 μ mol, 69%). Data for Product **A**: $[\alpha]_{\text{D}}^{22} -5.7$ (*c* 1.0, CH₂Cl₂); IR (cm⁻¹) 3064.3, 3031.6, 2927.4, 2856.1, 1496.5, 1455, 1250.6, 1177.3, 1145.5, 1012.5, 924.7, 862, 837; ¹H NMR (500 MHz, CDCl₃) δ 7.48 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.36 (d, *J* = 7.0 Hz, 2H), 7.31–7.23 (m, 11H), 5.97 (ddd, *J* = 17.5, 10.5, 5.0 Hz, 1H), 5.52 (s, 1H), 5.35 (d, *J* = 17.5 Hz, 1H), 5.18 (d, *J* = 10.0 Hz, 1H), 4.78 (d, *J* = 12.5 Hz, 1H), 4.67 (d, *J* = 12.5 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.52 (d, *J* = 11.5 Hz, 1H), 4.39 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.17 (d, *J* = 11.5 Hz, 1H), 3.86 (ddd, *J* = 11.0, 9.5, 5.0 Hz, 1H), 3.77 (dd, *J* = 12.0, 4.5 Hz, 1H), 3.64 (d, *J* = 11.0 Hz, 1H), 3.44 (d, *J* = 11.0 Hz, 1H), 3.24 (dd, *J* = 14.0, 1.0 Hz, 1H), 2.20–2.13 (m, 2H), 1.59 (ddd, *J* = 12.0, 12.0, 12.0 Hz, 1H), 1.41 (ddd, *J* = 13.0, 2.0, 2.0 Hz, 1H), 1.12 (s, 3H) 0.89 (s, 9H), 0.02 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 139.3, 139.1, 139.0, 138.3, 128.8 (2C), 128.46, 128.44, 128.2 (2C), 128.0 (2C), 127.7 (2C), 127.6, 127.3 (2C), 126.8 (2C), 115.8, 101.6, 78.3, 78.0, 76.3, 74.0, 73.65, 73.61, 73.5, 71.9, 65.4, 35.1, 32.5, 26.0 (3C), 18.1, 13.4, -4.0, -4.6; HRMS (ESI) calcd for C₃₉H₅₂O₆SiNa [M+Na] 667.3431, found 667.3409. Data for Product **B**: $[\alpha]_{\text{D}}^{22} -35.6$ (*c* 1.0, CH₂Cl₂); IR (cm⁻¹) 3443.3, 3031.6, 2925.5, 2868.6, 1496.5, 1454.1, 1342.2, 1309.4, 1211.1, 1143.6, 1090.6, 1027.9, 926.6, 839.8; ¹H NMR (500 MHz, CDCl₃) δ 7.48–7.46 (m, 2H), 7.33–7.24 (m, 13H), 5.95 (ddd, *J* = 17.0, 10.5, 5.0 Hz, 1H), 5.59 (s, 1H), 5.35 (ddd, *J* = 17.0, 1.5, 1.5 Hz, 1H), 5.20 (ddd, *J* = 10.5, 1.0, 1.0 Hz, 1H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 12.5 Hz, 1H), 4.43 (d, *J* = 12.0 Hz, 1H), 4.40 (m, 1H), 4.32 (ddd, *J* = 11.0, 3.0, 2.5 Hz, 1H), 3.85 (ddd, *J* = 11.0, 11.0, 5.0 Hz, 1H), 3.65 (ddd, *J* = 11.5, 11.5, 4.5 Hz, 1H), 3.55 (d, *J* = 11.0 Hz, 1H), 3.45 (d, *J* = 11.0 Hz, 1H), 3.05 (bs, 1H), 2.37 (ddd,

$J = 12.0, 4.5, 4.5$ Hz, 1H), 1.86 (ddd, $J = 11.5, 11.5, 11.5$ Hz, 1H), 1.74 (ddd, $J = 13.5, 2.5, 2.5$ Hz, 1H), 1.62 (ddd, $J = 12.0, 12.0, 12.0$ Hz, 1H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.0, 138.7, 138.2, 137.7, 129.2, 128.52 (2C), 128.51 (2C), 128.49 (2C), 127.8 (2C), 127.74 (2C), 127.71 (2C), 127.6, 126.3, 116.0, 101.6, 77.9 (2C), 77.6, 74.7, 73.6 (2C), 73.4, 71.4, 65.9, 32.9, 31.1, 13.5; HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{38}\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]$ 553.2566, found 553.2560.



(Z)-Ethyl 2-(((2R,3S,5R,6S)-5-(benzyloxy)-6-(benzyloxymethyl)-3-(tert-butyldimethylsilyloxy)-6-methyltetrahydro-2H-pyran-2-yl)methylene)-3-methylbutanoate. To a stirred solution of triethyl 2-phosphono-isopentrate (0.466 g, 1.75 mmol) in THF (10 mL) was added NaH (63 mg, 1.58 mmol) at 0 °C. After stirring for 10 min, a solution of aldehyde (0.170 g, 0.351 mmol) in THF (25 mL) was added dropwise at 0 °C under argon atmosphere. After stirring at rt for 14 h, saturated aqueous NH_4Cl was added at 0 °C, and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by flash column chromatography (*n*-hexane:EtOAc = 5:1→3:1) to give ester (0.111 g, 53% yield). $[\alpha]_{\text{D}}^{22} +29.3$ (c 1.0, CH_2Cl_2); IR (cm^{-1}) 3087.5, 3063.4, 3030.6, 2959.2, 1948.7, 1721.2, 1659.5, 1604.5, 1496.5, 1462.7, 1363.4, 1221.7, 1094.4, 939.2, 906.4, 837; ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.23 (m, 10H), 5.54 (dd, $J = 8.5, 1.5$ Hz, 1H), 4.63 (d, $J = 12.5$ Hz, 1H), 4.53 (d, $J = 11.5$ Hz, 1H), 4.52 (d, $J = 12.5$ Hz, 1H), 4.44 (dd, $J = 8.5, 8.5$ Hz, 1H), 4.42 (d, $J = 12.0$ Hz, 1H), 4.24–4.13 (m, 2H), 3.75 (dd, $J = 12.0, 5.0$ Hz, 1H), 3.53 (d, $J = 10.0$ Hz, 1H), 3.43 (d, $J = 10.0$ Hz, 1H), 3.36 (ddd, $J = 11.0, 9.5, 5.0$ Hz, 1H), 2.70

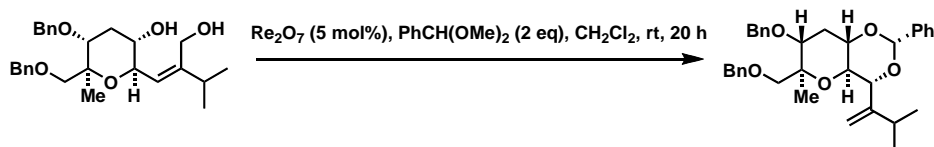
(dquin, $J = 7.0, 7.0, 7.0, 7.0, 1.5$ Hz, 1H), 2.16 (ddd, $J = 12.0, 4.5, 4.5$ Hz, 1H), 1.59 (ddd, $J = 12.5, 12.5, 12.5$ Hz, 1H), 1.28 (dd, $J = 7.0, 7.0$ Hz, 1H), 1.17 (s, 3H), 1.06 (dd, $J = 7.0, 4.5$ Hz, 6H), 0.83 (s, 9H), 0.00 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 168.9, 143.4, 138.9, 138.8, 130.8, 128.7 (2C), 128.1 (2C), 127.8 (2C), 127.71 (2C), 127.67 (2C), 77.4, 74.6, 73.8, 73.6, 72.1, 71.6, 70.7, 60.4, 35.2, 32.0, 25.9 (3C), 21.5, 21.0, 18.1, 14.4, 13.9, -4.1, -4.4; HRMS (ESI) calcd for $\text{C}_{35}\text{H}_{52}\text{O}_6\text{SiNa}$ $[\text{M}+\text{Na}]$ 619.3424, found 619.3425.



(2*R*,3*S*,5*R*,6*S*)-5-(benzyloxy)-6-(benzyloxymethyl)-2-((*Z*)-2-(hydroxymethyl)-3-methylbut-1-enyl)-6-methyltetrahydro-2*H*-pyran-3-ol. To a solution of α,β -unsaturated ester (46.0 mg, 77 μmol) in CH_2Cl_2 (0.8 mL) was added DIBALH (1.0 M in toluene, 0.23 mL, 0.23 mmol) at -78°C under argon atmosphere. After stirring at the same temperature for 1 h, *i*-PrOH, H_2O , SiO_2 , Celite and CH_2Cl_2 were added, and the mixture was warmed to rt. The mixture was stirred at rt for 1 h and magnesium sulfate was added. The mixture was filtered through Celite pad and the filtrate was concentrated *in vacuo*, and the residue was submitted to the next reaction without further purification.

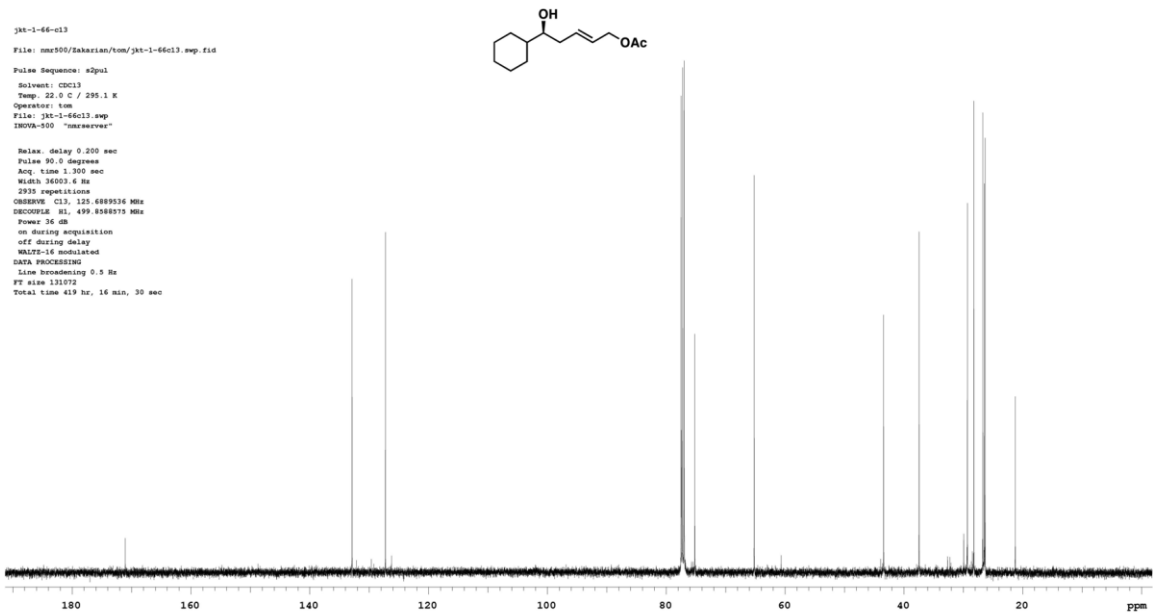
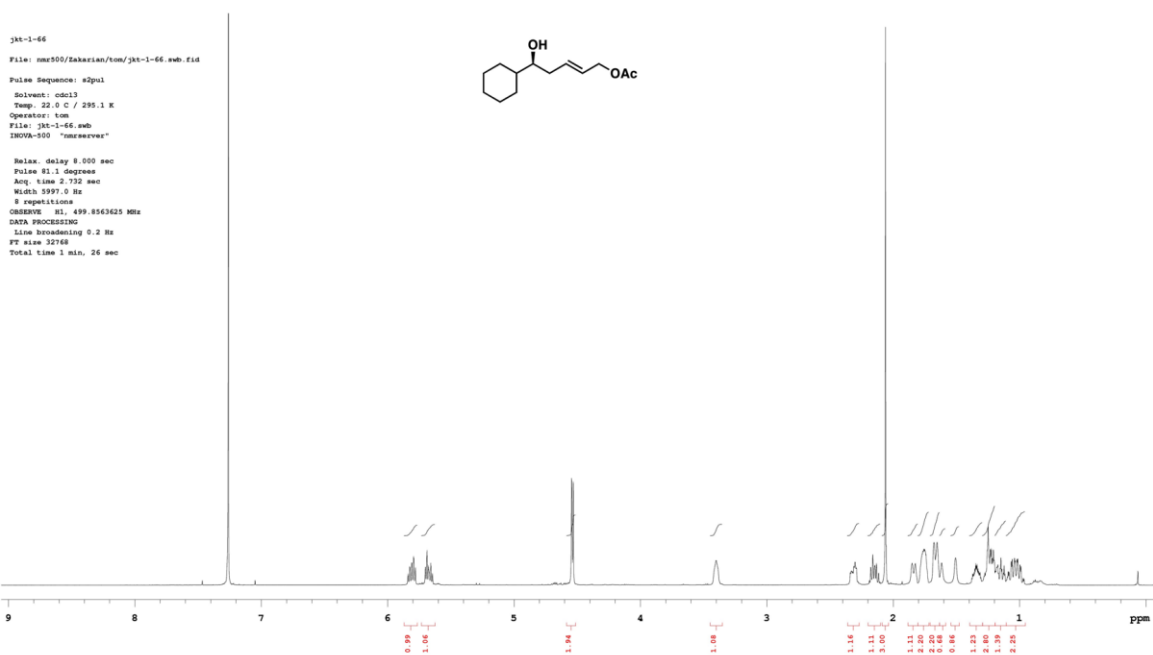
To a solution of the crude was added TBAF (1.0 M in THF, 0.16 mL, 0.16 mmol) at room temperature. After stirring for 1 h, water was added and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, hexane:EtOAc = 2:1) to give diol (30.0 mg, 88% yield, 2 steps). $[\alpha]_{\text{D}}^{22} +7.6$ (c 1.0, CH_2Cl_2); IR (cm^{-1}) 3348.8, 3063.4, 3029.6, 3958.3, 2870.5, 1496.5, 1454.1, 1365.4, 1234.2, 1207.2, 1104.1, 1027.9, 903.5; ^1H NMR

(500 MHz, CDCl₃) δ 7.33–7.22 (m, 10H), 5.38 (d, J = 7.5 Hz, 1H), 4.61 (d, J = 12.5 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.52 (d, J = 12.5 Hz, 1H), 4.41 (d, J = 12.0 Hz, 1H), 4.18 (dd, J = 9.5, 8.0 Hz, 1H), 4.02 (d, J = 12.0 Hz, 1H), 3.74 (dd, J = 11.5, 4.5 Hz, 1H), 3.51 (d, J = 10.0 Hz, 1H), 3.45 (d, J = 10.0 Hz, 1H), 3.38 (ddd, J = 11.0, 9.5, 4.5 Hz, 1H), 2.41 (dqin, J = 7.0, 7.0, 7.0, 7.0, 1.0 Hz, 1H), 2.38 (ddd, J = 12.0, 4.5, 4.5 Hz, 1H), 1.66 (ddd, J = 12.0, 12.0, 12.0 Hz, 1H), 1.24 (s, 3H), 1.08 (dd, J = 7.0, 1.5 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 151.2, 138.64, 138.58, 128.5 (2C), 128.0 (2C), 127.8 (2C), 127.7 (2C), 125.3, 77.6, 74.7, 73.9, 73.7, 71.7, 71.5, 69.3, 59.8, 35.0, 33.7, 21.7, 13.7; HRMS (ESI) calcd for C₂₇H₃₆O₅Na [M+Na] 463.2460, found 463.2448.

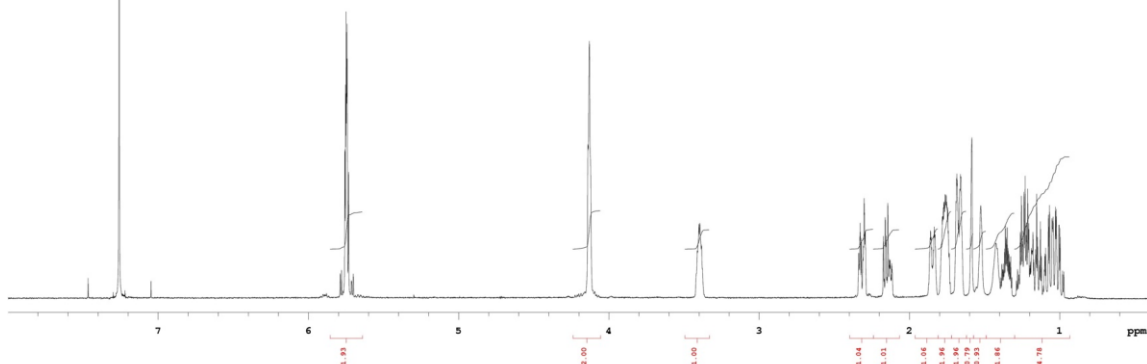
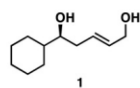


(2*S*,4*R*,4*aS*,6*S*,7*R*,8*aS*)-7-(benzyloxy)-6-(benzyloxymethyl)-6-methyl-4-(3-methyl-but-1-en-2-yl)-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxine. Following the typical procedure, to a solution of diol (15.0 mg, 0.034 mmol) and benzaldehyde dimethyl acetal (10 μ L, 0.068 mmol) in CH₂Cl₂ (0.35 mL) was added rhenium(VII) oxide (0.8 mg, 1.7 μ mol) under argon atmosphere. After stirring at the same temperature for 20 h, saturated aqueous NaHCO₃ was added at 0 °C, and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, hexane:EtOAc = 10:1→5:1) to give the product (17.4 mg, 97% yield). [α]_D²² -1.9 (*c* 1.0, CH₂Cl₂); IR (cm⁻¹) 2923.6, 1496.5, 1457.9, 1369.2, 1284.4, 1207.2, 1095.4, 1025.9, 910.2, 806.1; ¹H NMR (500 MHz, CDCl₃) δ 7.52–7.50 (m, 2H), 7.36–7.27 (m, 13H), 5.64 (s, 1H), 5.23 (s, 1H), 5.08 (s, 1H), 4.61 (d, J = 11.5 Hz, 1H), 4.58 (s, 1H), 4.46 (d, J = 11.5 Hz, 1H), 4.14 (d, J

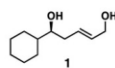
= 9.0 Hz, 1H), 3.86 (dd, J = 12.0, 5.0 Hz, 1H), 3.58 (ddd, J = 12.0, 9.5, 4.5 Hz, 1H), 3.54 (d, J = 10.5 Hz, 1H), 3.46 (dd, J = 9.0, 9.0 Hz, 1H), 3.45 (d, J = 11.0 Hz, 1H), 2.52 (quin, J = 7.0 Hz, 1H), 2.45 (ddd, J = 11.0, 4.0, 4.0 Hz, 1H), 1.79 (ddd, J = 11.5, 11.5, 11.5 Hz, 1H), 1.19 (s, 3H), 1.10 (d, J = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.2, 139.0, 138.6, 138.0, 129.1, 128.53 (2C), 128.49 (2C), 128.45 (2C), 127.81 (2C), 127.77 (2C), 127.7 (2C), 127.6, 126.5, 111.1, 101.5, 82.2, 79.0, 76.9, 74.6, 74.1, 73.7, 71.5, 71.2, 30.80, 30.78, 23.0, 22.8, 14.0; HRMS (ESI) calcd for $\text{C}_{34}\text{H}_{40}\text{O}_5\text{Na}$ [$\text{M}+\text{Na}$] 551.2768, found 551.2775.



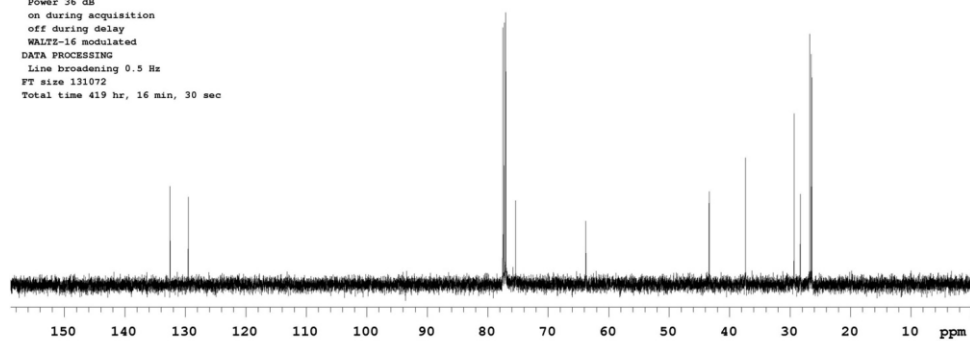
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 Operator: stivala
 File: ces-5-159-2.exp
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 Relax. delay 8.000 sec
 Pulse P1: 1.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

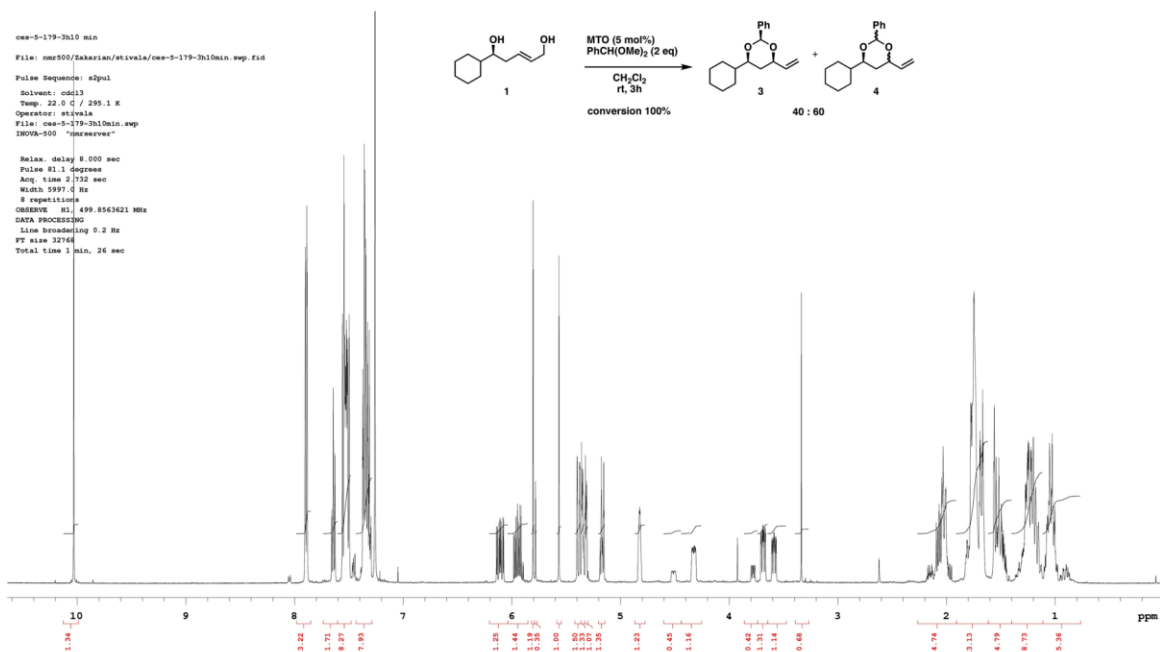
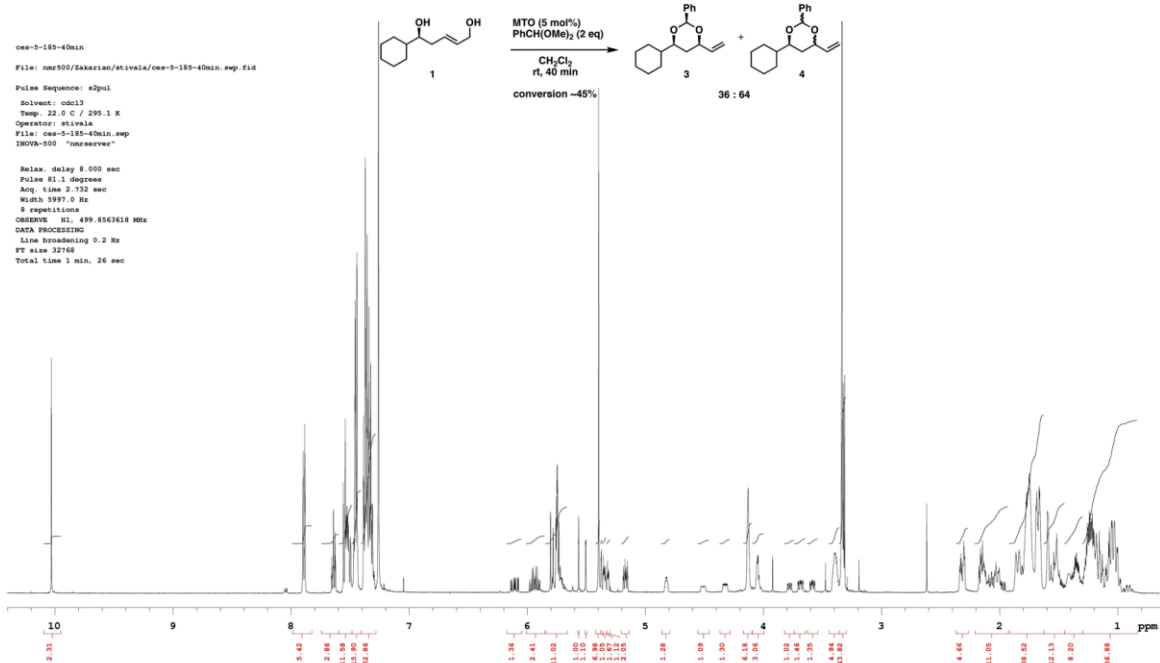


ces-5-159-cl3
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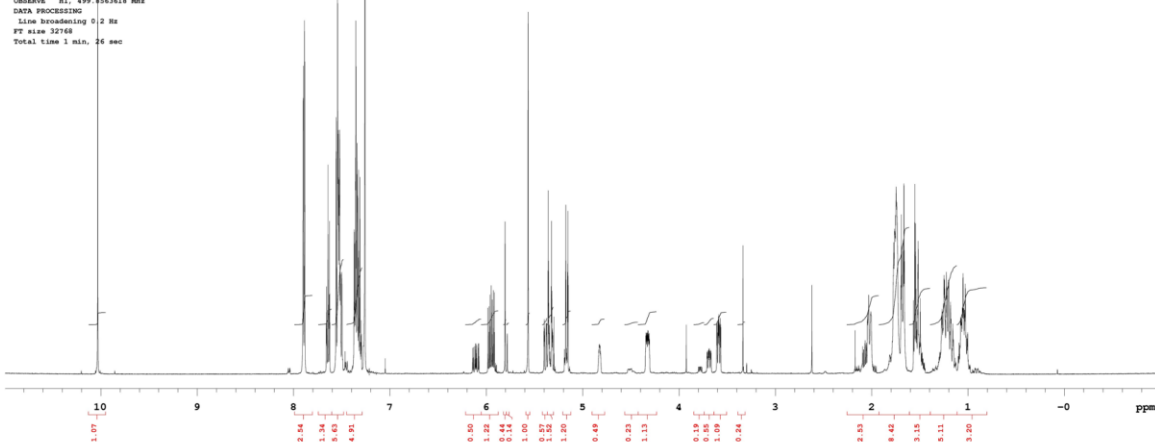


Relax. delay 0.200 sec
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 Width 36003.6 Hz
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 DECOUPLE H1, 499.8588575 MHz
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 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
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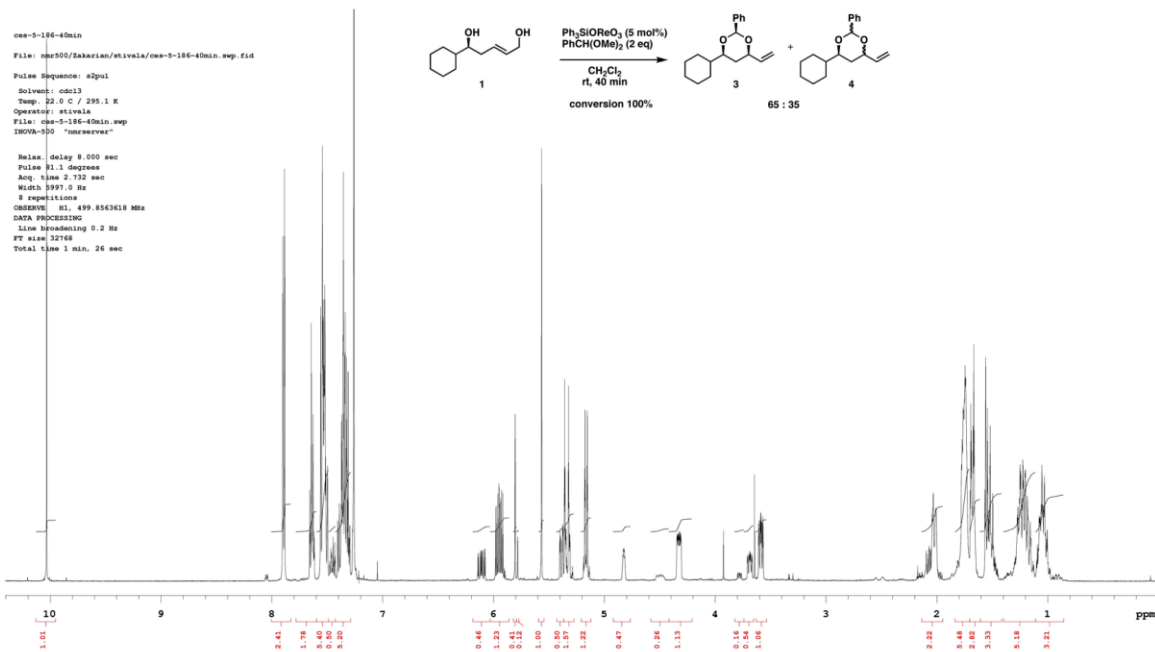




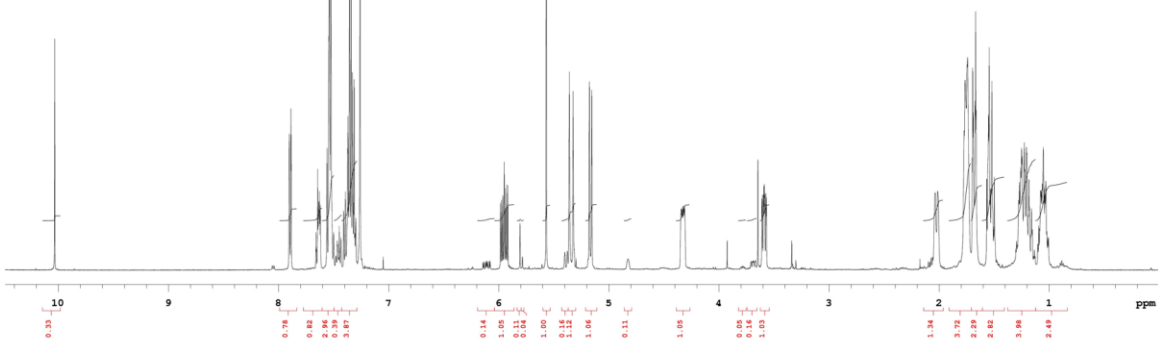
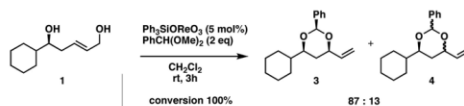
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 Temp: 22.0 C / 295.1 K
 Operator: etivale
 File: cea-5-179-20h.swp
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 Relax: delay 8.000 sec
 Pulse 81.1 degrees
 Acq: time 2.732 sec
 Width 5997.0 Hz
 S repetitions
 CDSAMP: 80.489.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



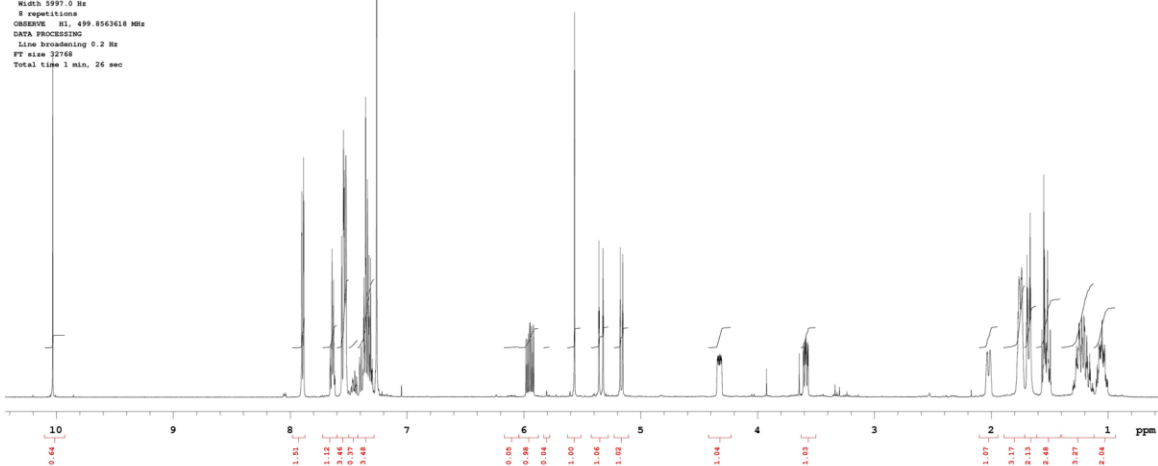
cea-5-186-40min
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 Operator: etivale
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 Relax: delay 8.000 sec
 Pulse 81.1 degrees
 Acq: time 2.732 sec
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 S repetitions
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 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

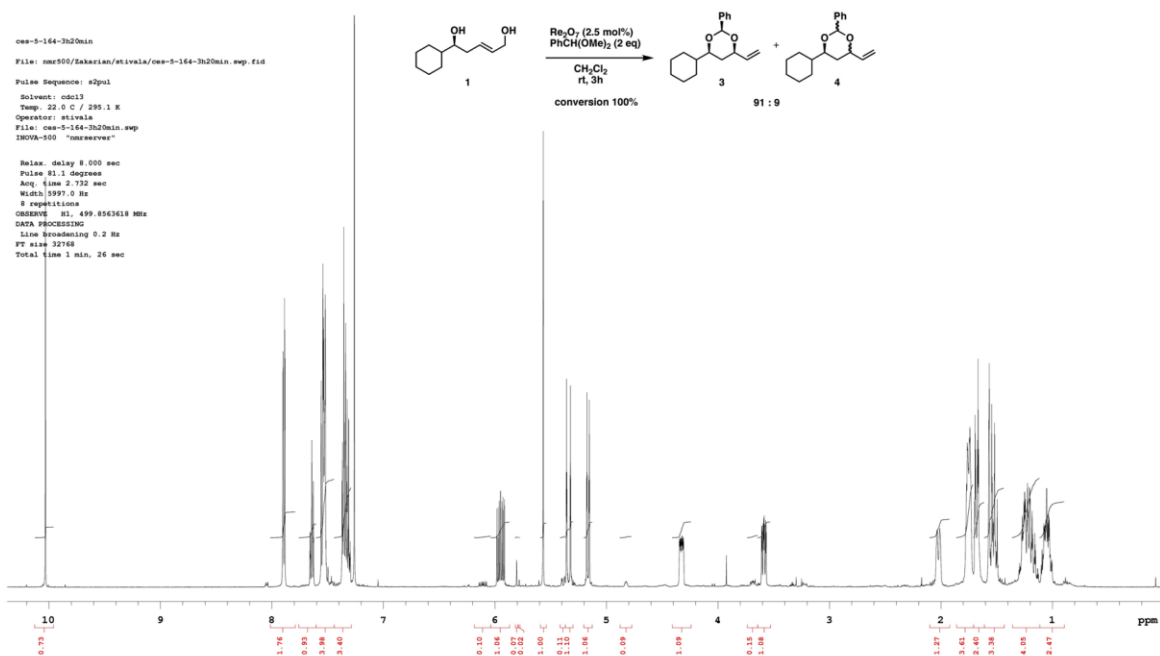
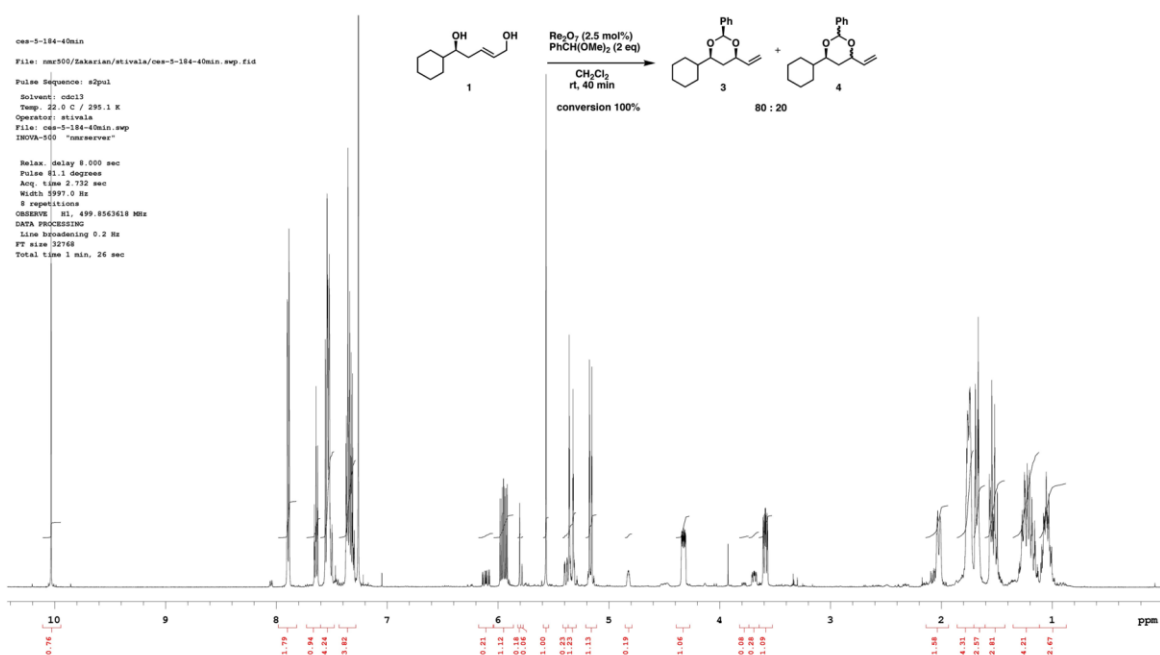


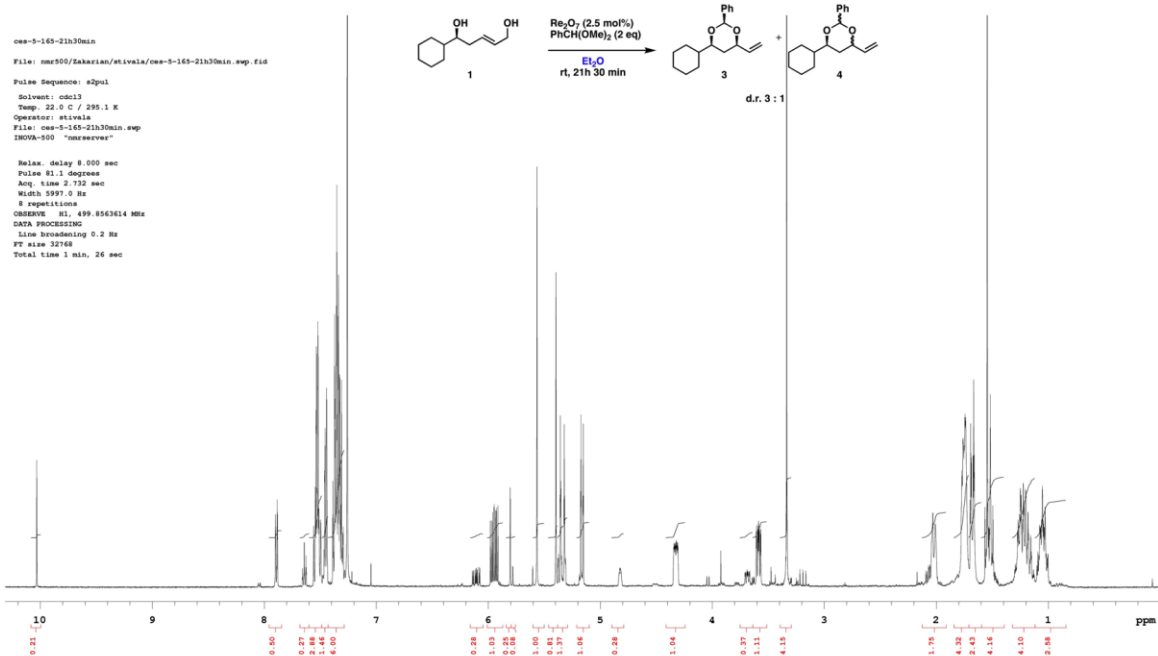
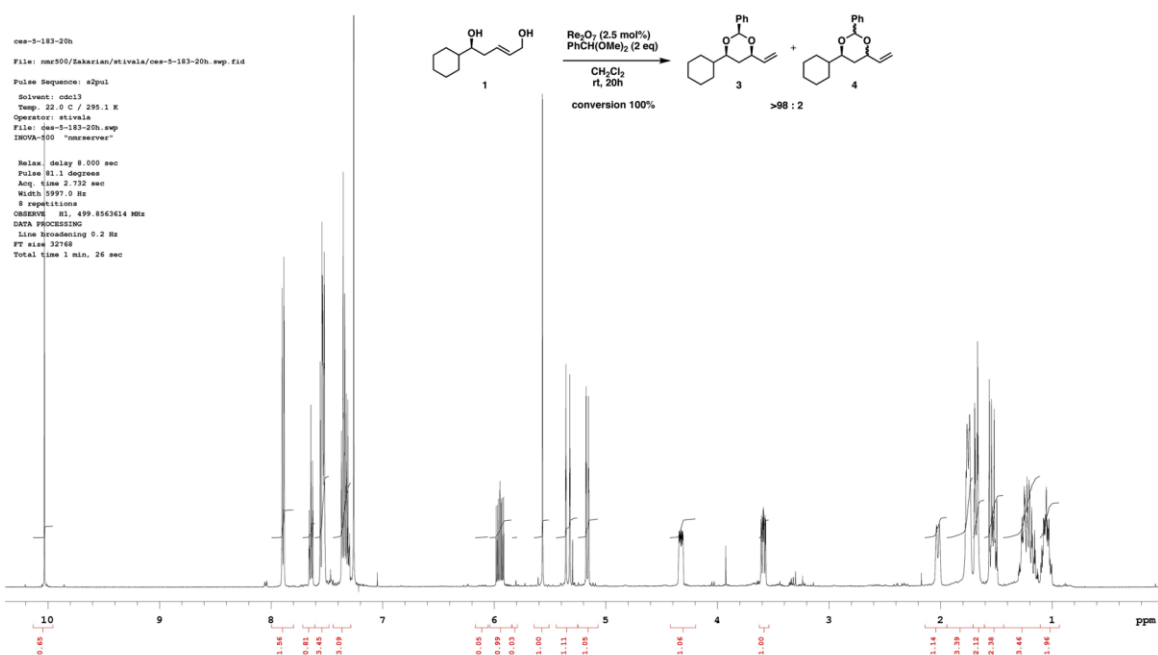
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 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivale
 File: cea-5-180-3h10min.exp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
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 S repetitions
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 Line Broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

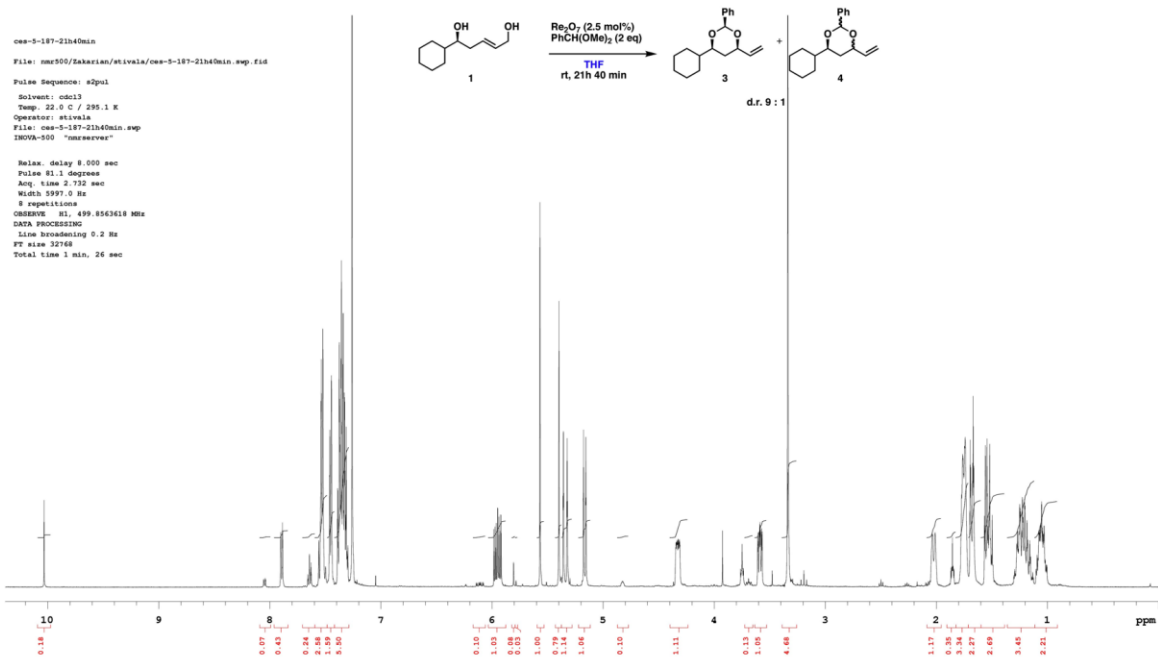
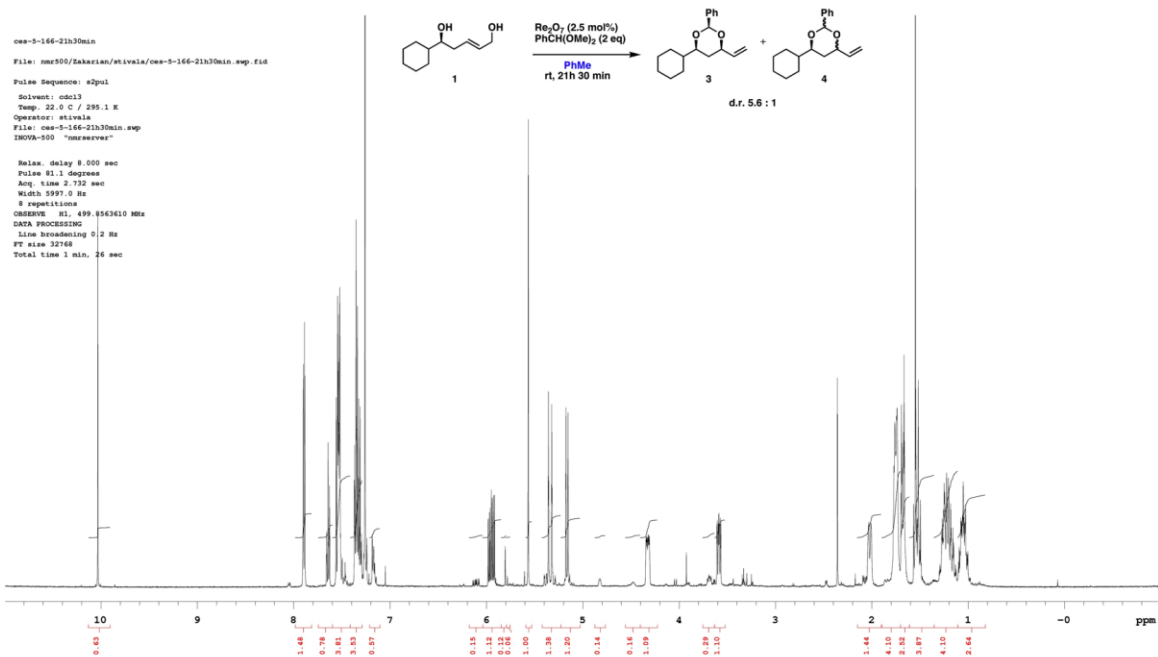


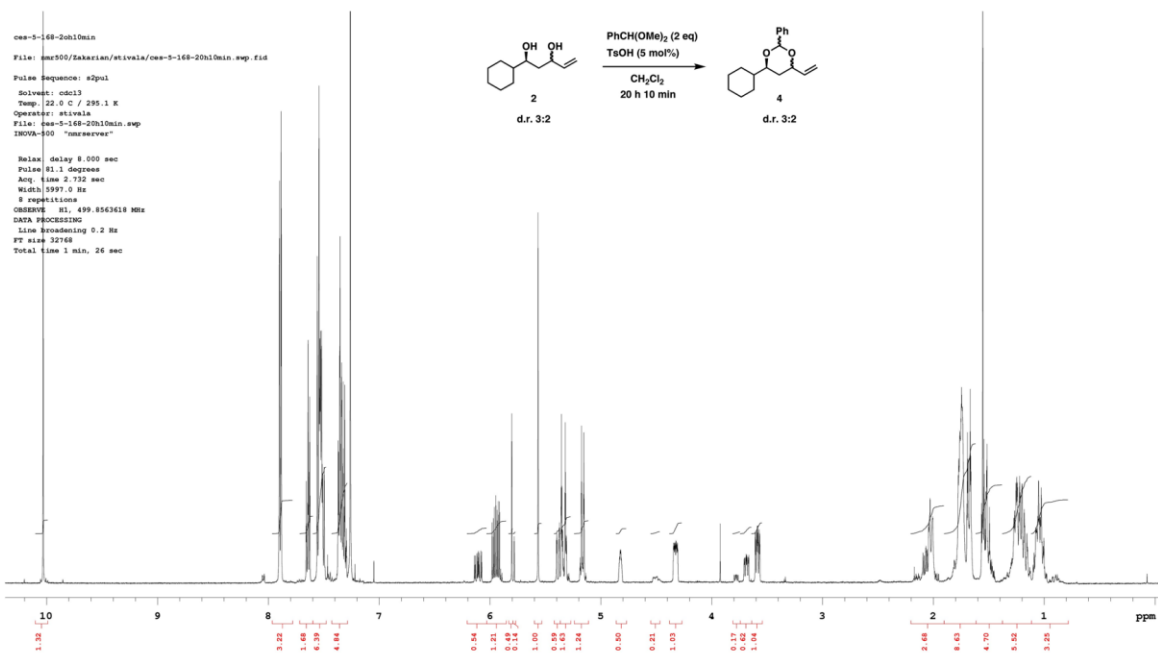
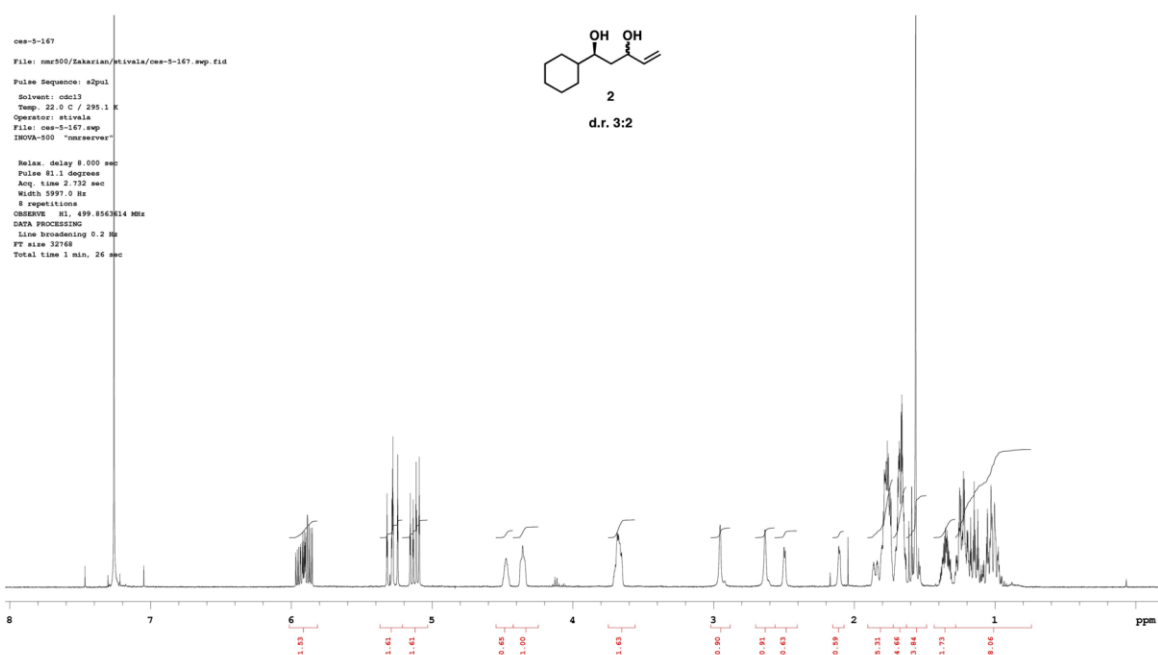
cea-5-180-20h
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 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivale
 File: cea-5-180-20h.exp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 S repetitions
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 DATA PROCESSING
 Line Broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

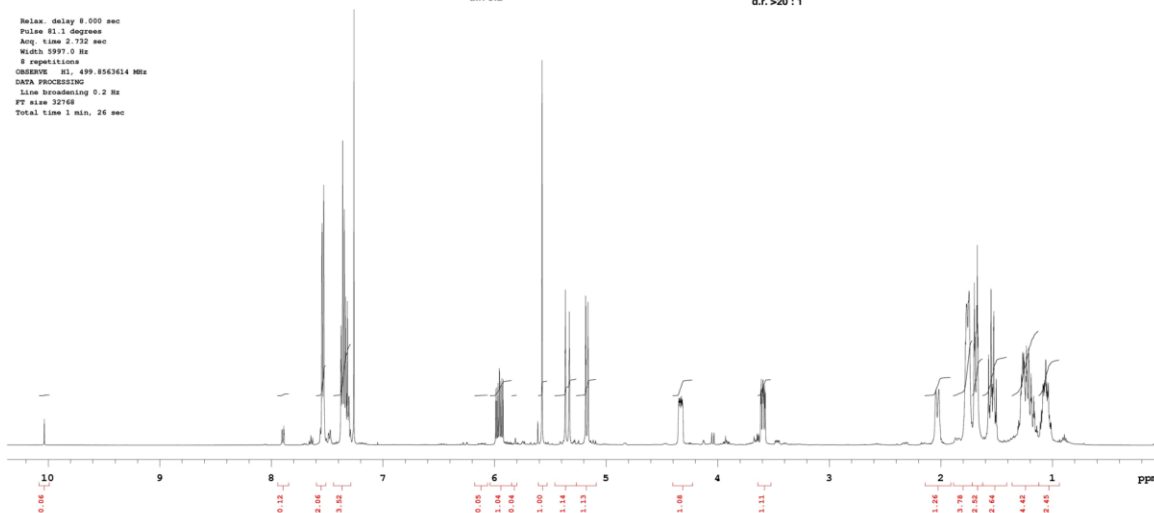




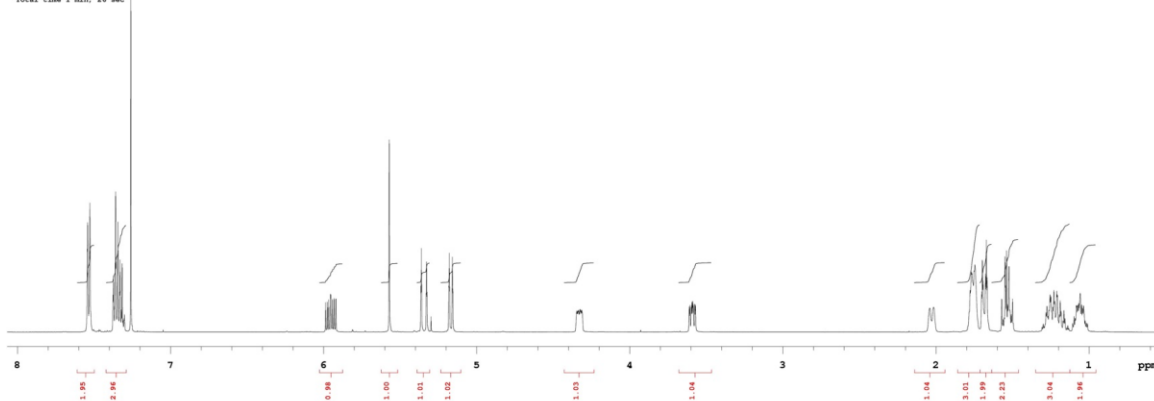








Chemical structure of compound **3**: A 1,3-dioxolane ring substituted with a phenyl group (Ph) at position 4, a cyclohexyl group at position 2, and a vinyl group at position 5.



ces-5-183-cl3

File: nmr500/Zakarian/stivala/ces-5-183-cl3.swp.fid

Pulse Sequence: s2pul

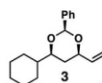
Solvent: CDCl3

Temp. 22.0 C / 295.1 K

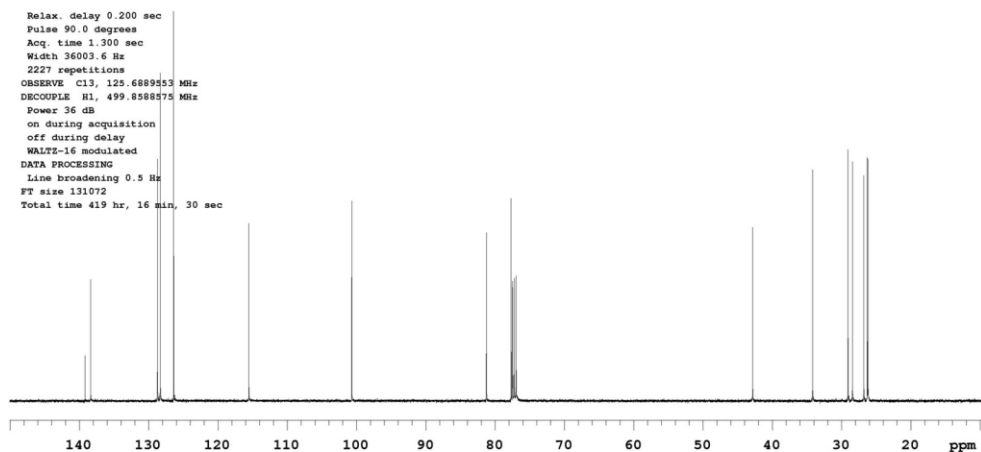
Operator: stivala

File: ces-5-183-cl3.swp

INOVA-500 "nmrserver"



Relax. delay 0.200 sec
Pulse 90.0 degrees
Acq. time 1.300 sec
Width 36003.6 Hz
2227 repetitions
OBSERVE C13, 125.6889553 MHz
DECOUPLE H1, 499.8588575 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 419 hr, 16 min, 30 sec



ces-5-234-noe

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Pulse Sequence: cyclenoe

Solvent: cdcl3

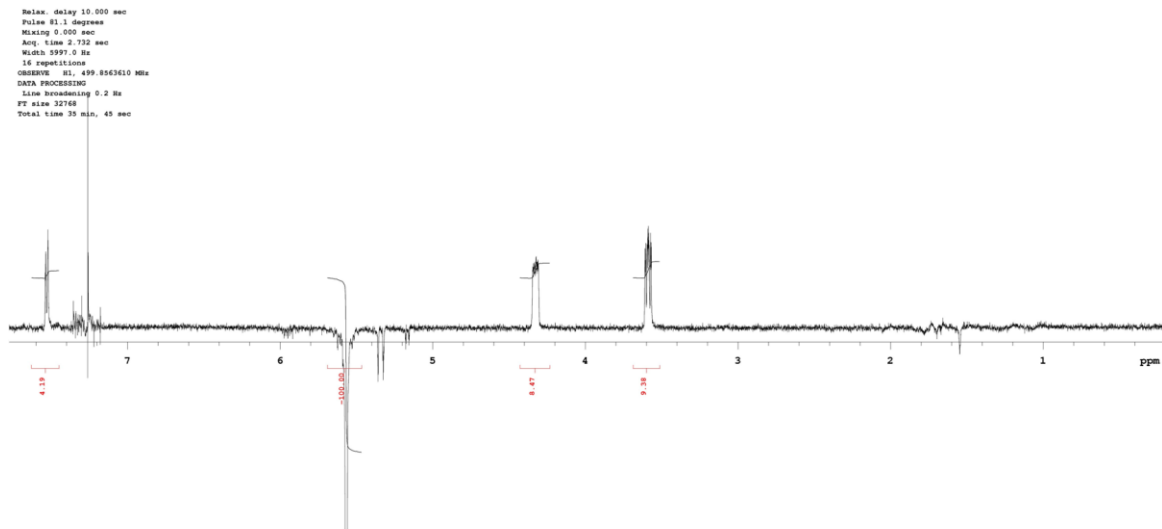
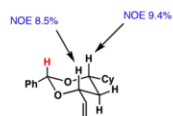
Temp. 22.0 C / 295.1 K

Operator: stivala

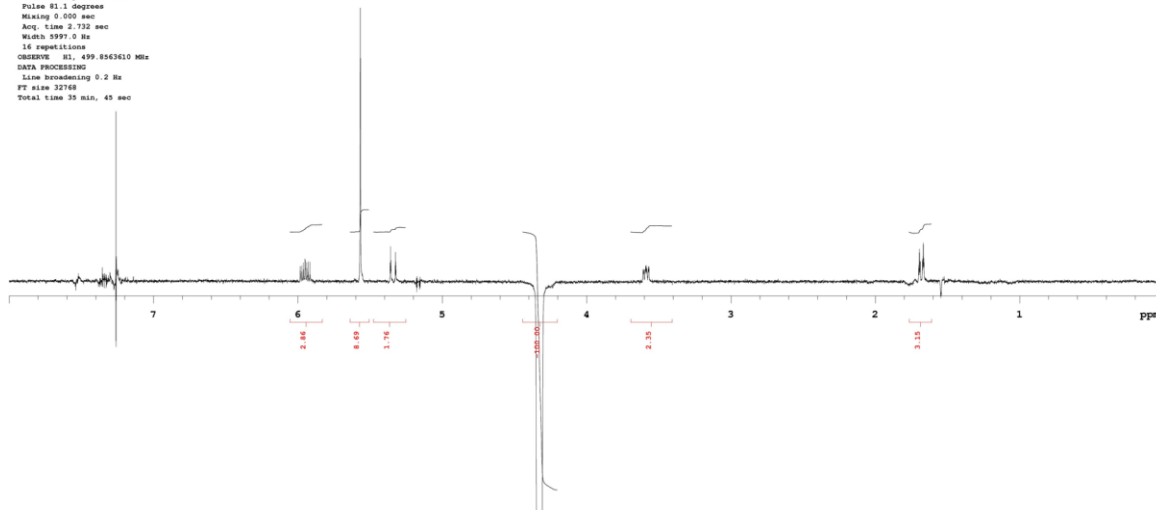
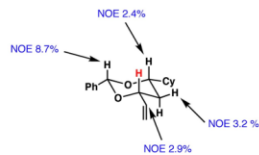
File: ces-5-234-noe.swp

INOVA-500 "nmrserver"

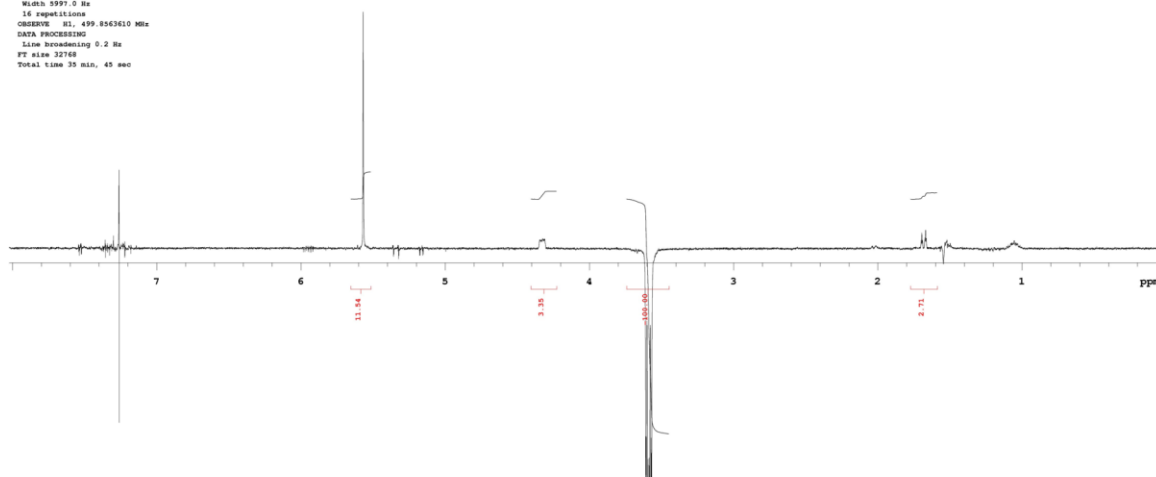
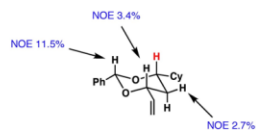
Relax. delay 10.000 sec
Pulse 81.1 degrees
Mixing 0.000 sec
Acq. time 2.730 sec
Width 5997.0 Hz
18 repetitions
OBSERVE H1, 499.8563610 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 35 min, 45 sec



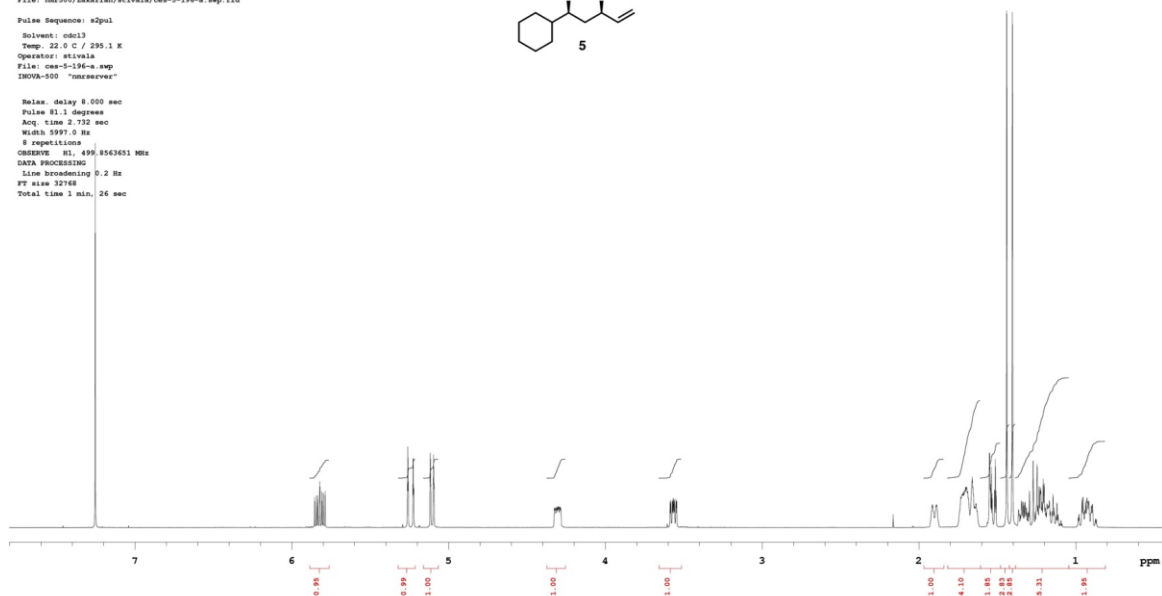
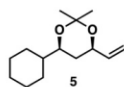
cea-5-234-nm
 File: nmr505/Sakarian/etivala/cea-5-234-nm.exp.fid
 Pulse Sequence: cyclopmo
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-234-nm.exp
 INOVA-500 "nmserver"
 Relax: delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563610 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 35 min, 45 sec



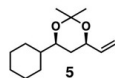
cea-5-234-nm
 File: nmr505/Sakarian/etivala/cea-5-234-nm.exp.fid
 Pulse Sequence: cyclopmo
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-234-nm.exp
 INOVA-500 "nmserver"
 Relax: delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563610 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 35 min, 45 sec



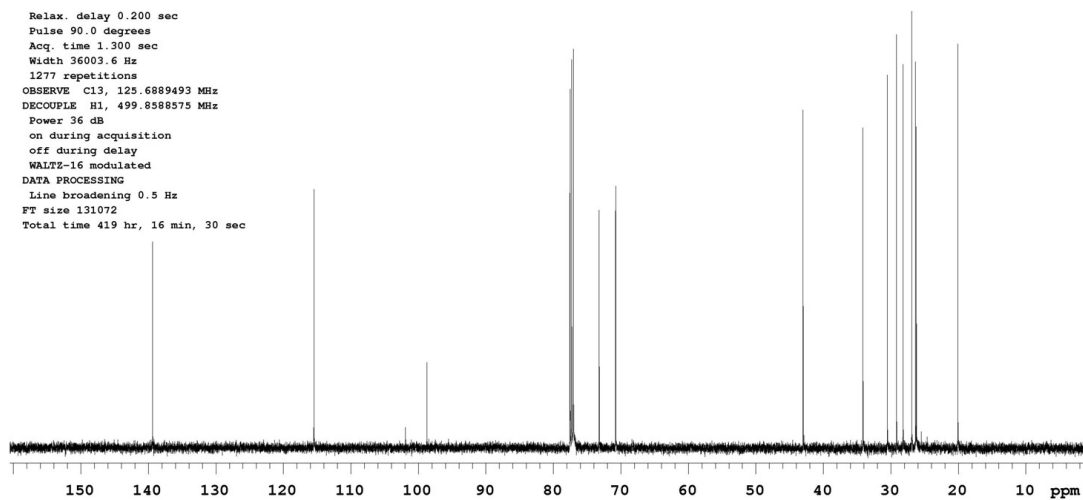
ces-5-196-a
 File: nmr500/Zakarian/stivala/ces-5-196-a.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivala
 File: ces-5-196-a.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563651 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

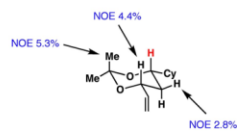
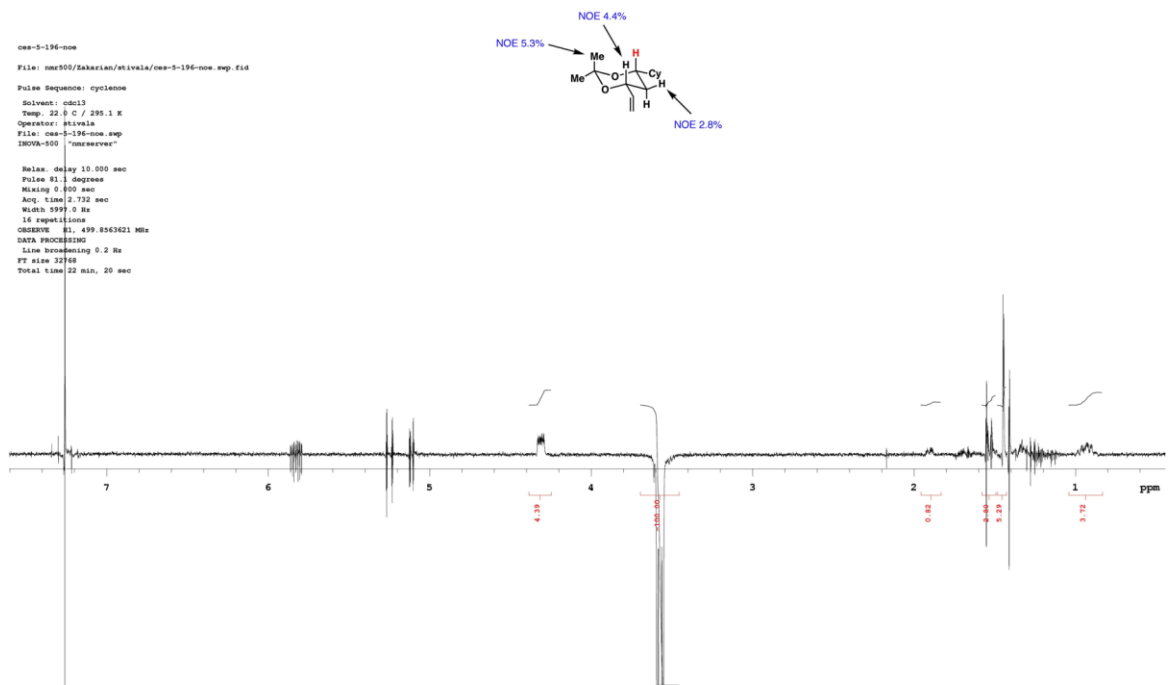
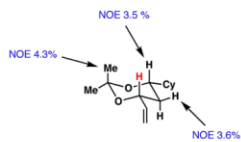
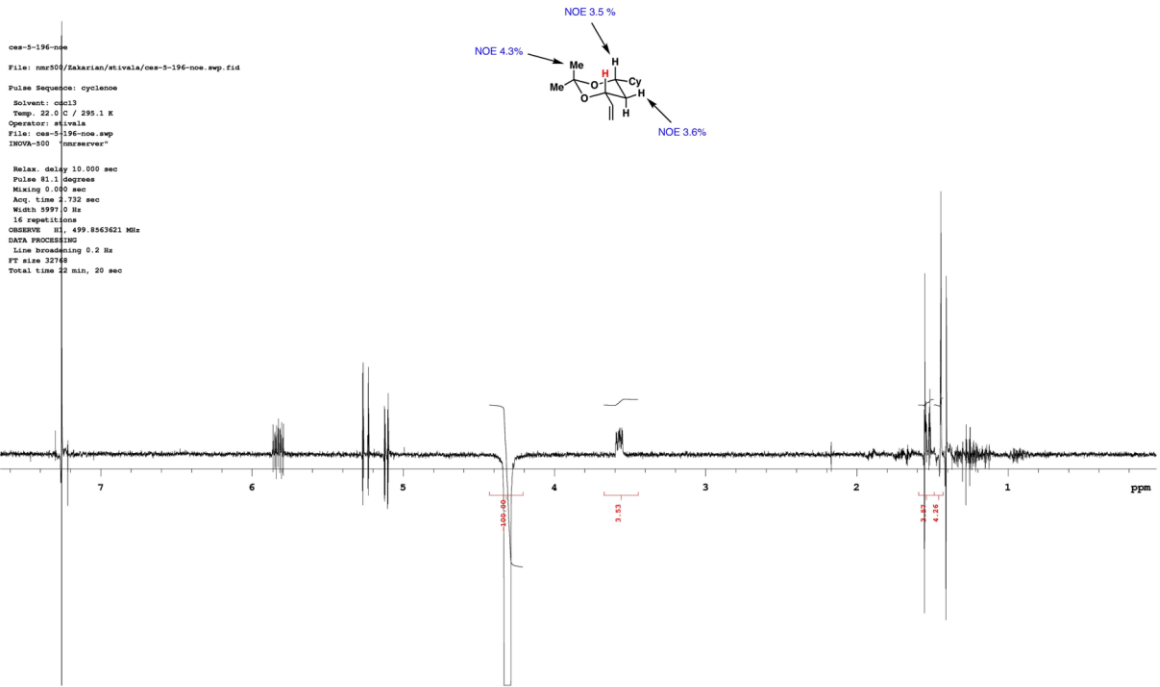


ces-5-196-a-cl3
 File: nmr500/Zakarian/stivala/ces-5-196-a-cl3.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDC13
 Temp: 22.0 C / 295.1 K
 Operator: stivala
 File: ces-5-196-a-cl3.swp
 INOVA-500 "nmrserver"

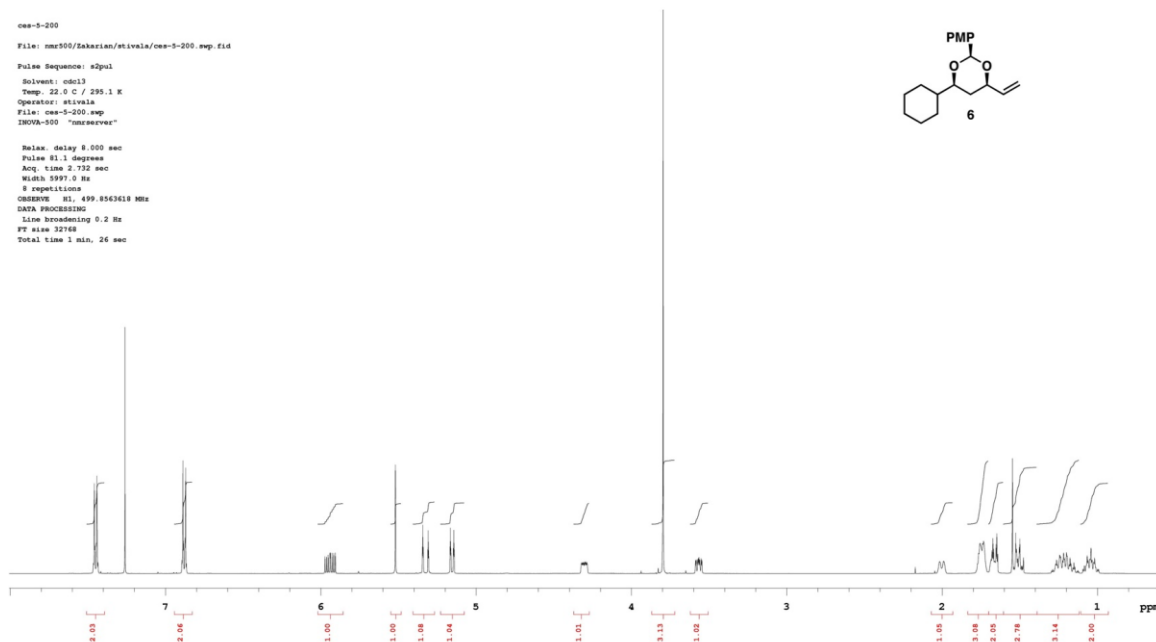
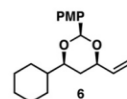


Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 1277 repetitions
 OBSERVE C13, 125.6889493 MHz
 DECOUPLE H1, 499.8588575 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 131072
 Total time 419 hr, 16 min, 30 sec





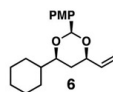
ces-5-200
 File: nmr500/Zakarian/stivala/ces-5-200.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivala
 File: ces-5-200.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



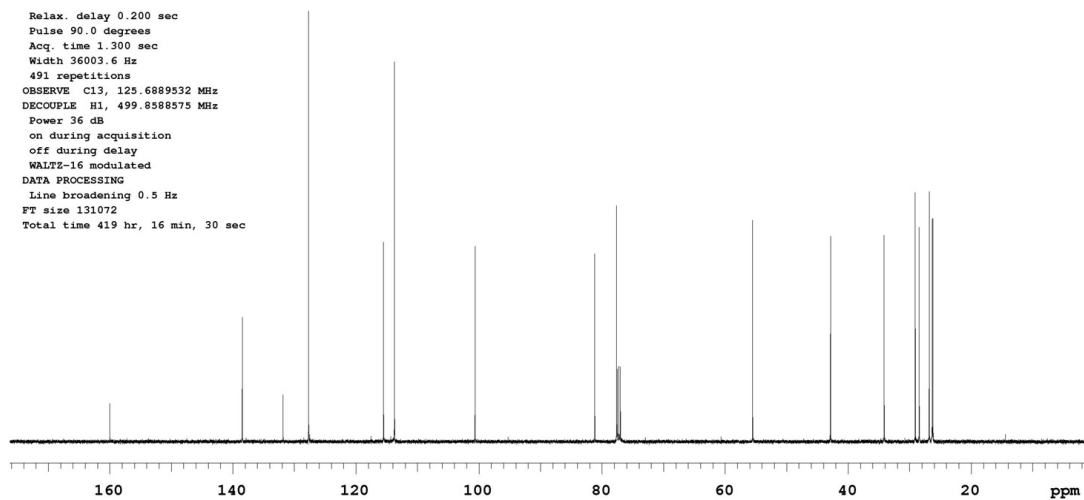
ces-5-200-cl3

File: nmr500/Zakarian/stivala/ces-5-200-cl3.swp.fid

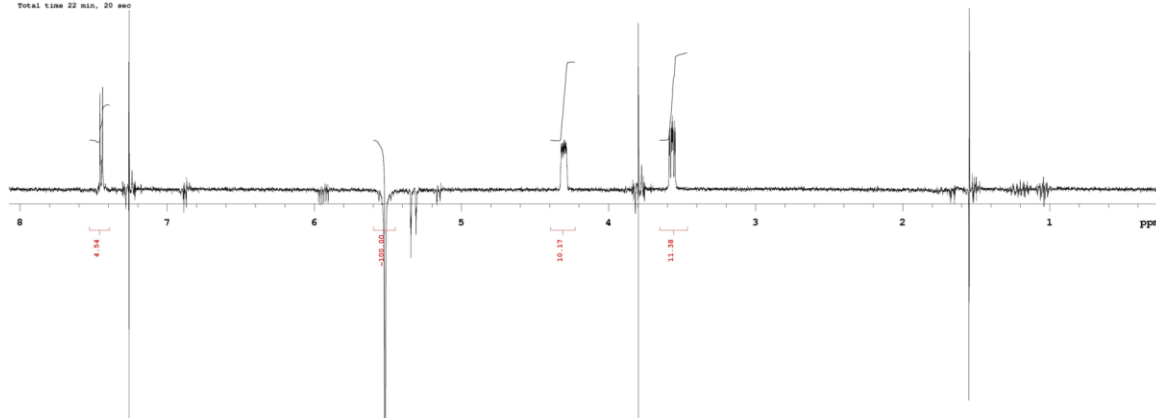
Pulse Sequence: s2pul
 Solvent: CDC13
 Temp: 22.0 C / 295.1 K
 Operator: stivala
 File: ces-5-200-cl3.swp
 INOVA-500 "nmrserver"



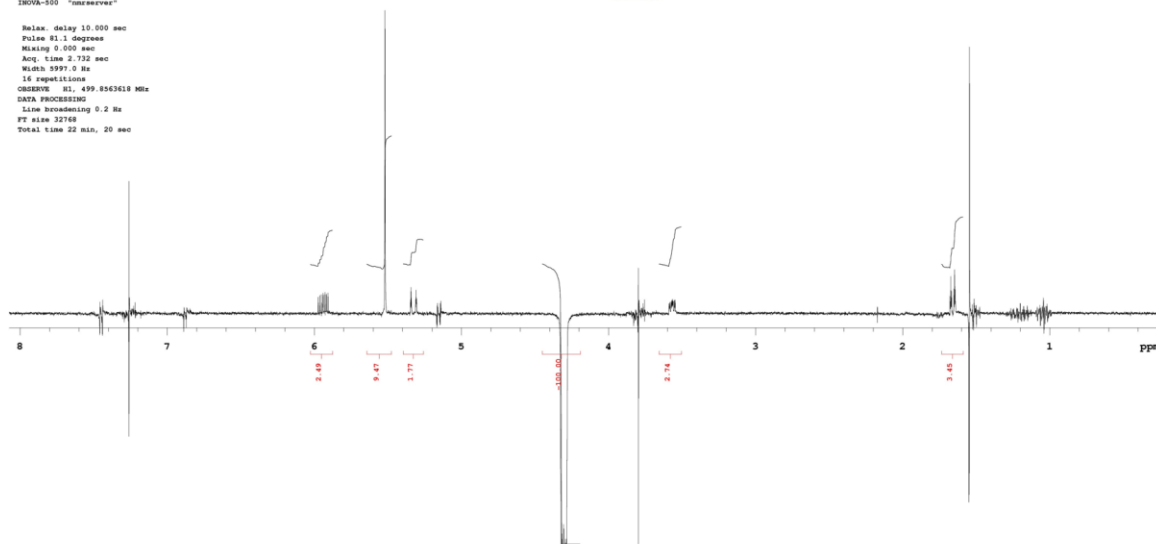
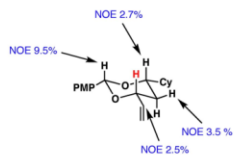
Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 491 repetitions
 OBSERVE C13, 125.6889832 MHz
 DECOUPLE H1, 499.8588575 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 131072
 Total time 419 hr, 16 min, 30 sec

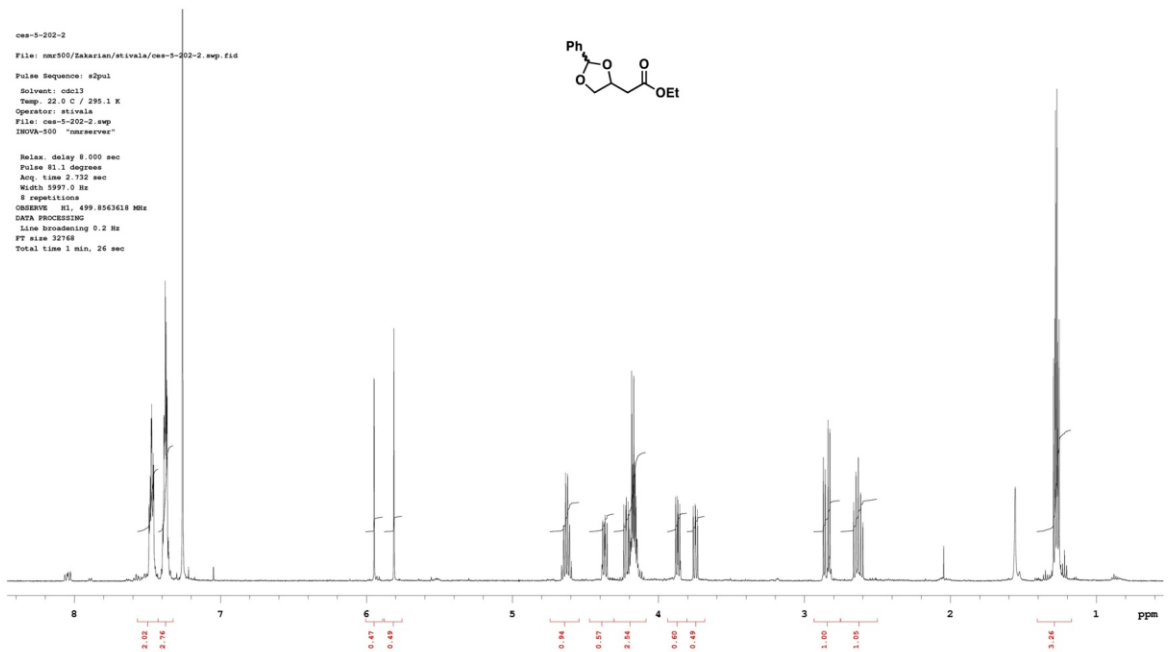
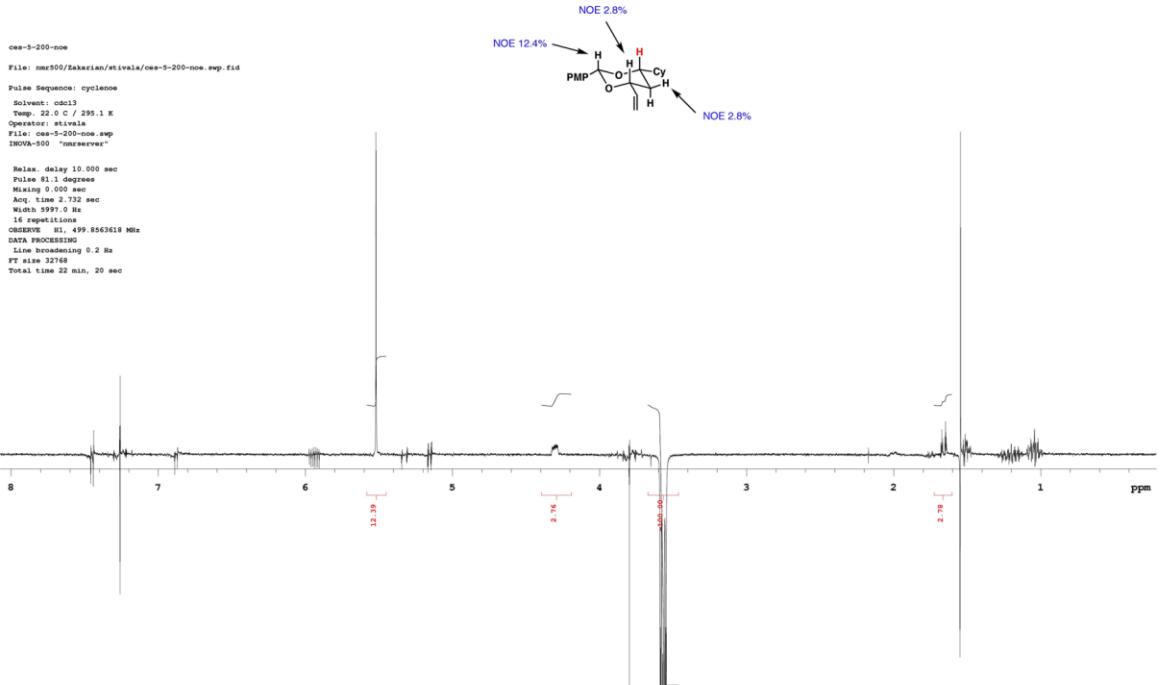


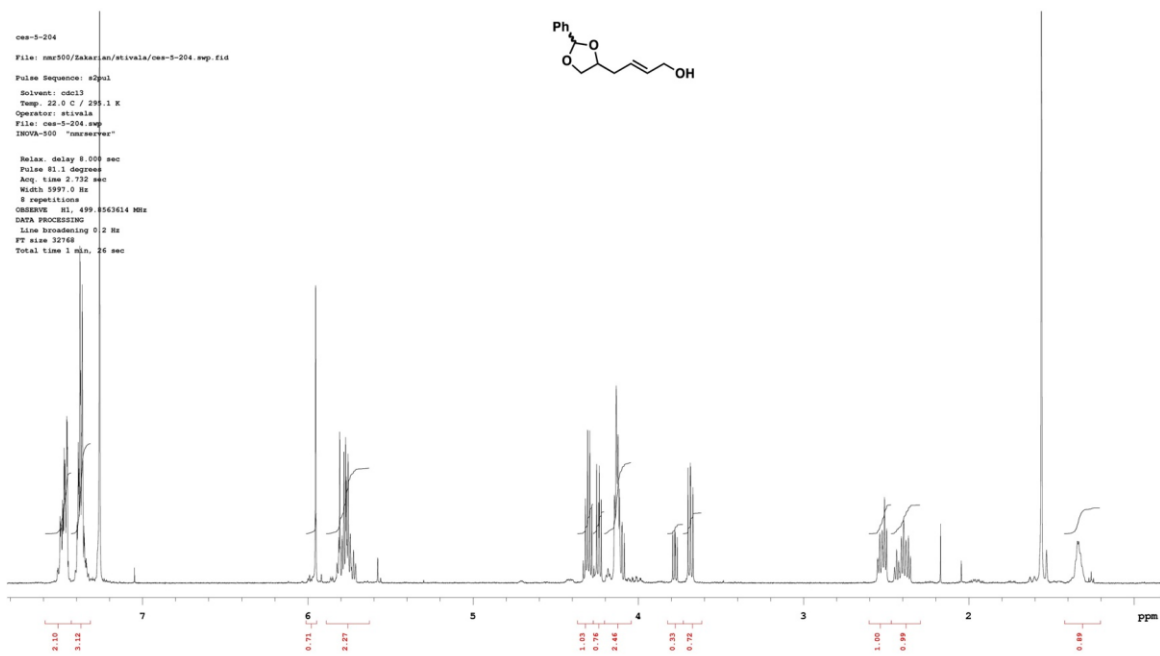
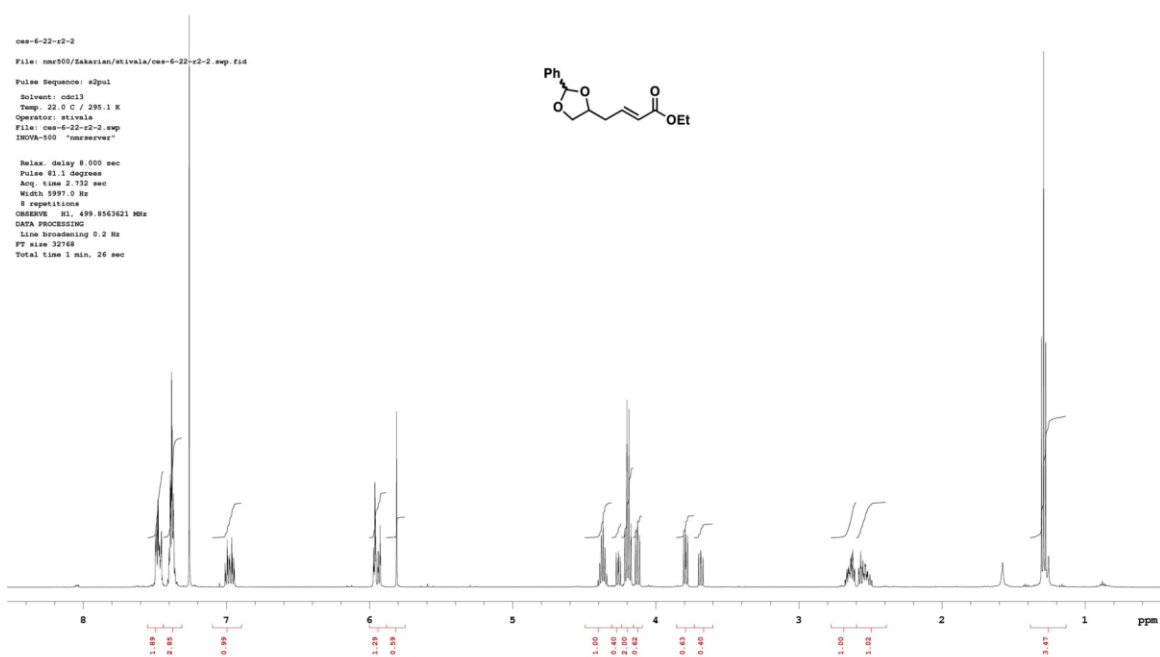
cea-3-200-nmr
 File: nmr505/Sakarian/etivala/cea-3-200-nmr.exp.fid
 Pulse Sequence: cyclohex
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-3-200-nmr.exp
 INOVA-500 "nmrserver"
 Relax: delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 22 min, 20 sec



cea-3-200-nmr
 File: nmr505/Sakarian/etivala/cea-3-200-nmr.exp.fid
 Pulse Sequence: cyclohex
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-3-200-nmr.exp
 INOVA-500 "nmrserver"
 Relax: delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 22 min, 20 sec







ces-5-208

File: nmr500/Zakarian/stivala/ces-5-208.swp.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp: 22.0 C / 295.1 K

Operator: stivala

File: ces-5-208.swp

INOVA-500 "nmrserver"

Relax. delay 8.000 sec

Pulse 81.1 degrees

Acq. time 2.732 sec

Width 5997.0 Hz

8 repetitions

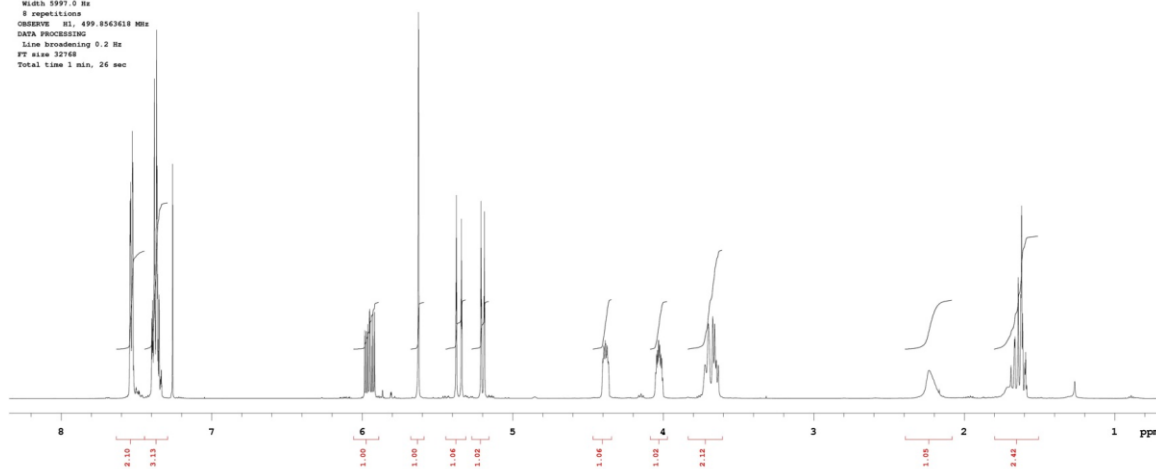
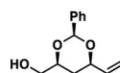
OBSERVE H1, 499.8563618 MHz

DATA PROCESSING

Line broadening 0.2 Hz

FT size 32768

Total time 1 min, 26 sec



ces-5-208-cl3

File: nmr500/Zakarian/stivala/ces-5-208-cl3.swp.fid

Pulse Sequence: s2pul

Solvent: CDC13

Temp: 22.0 C / 295.1 K

Operator: stivala

File: ces-5-208-cl3.swp

INOVA-500 "nmrserver"

Relax. delay 0.200 sec

Pulse 90.0 degrees

Acq. time 1.300 sec

Width 36003.6 Hz

1432 repetitions

OBSERVE C13, 125.6889600 MHz

DECOUPLE H1, 499.8588575 MHz

Power 36 dB

on during acquisition

off during delay

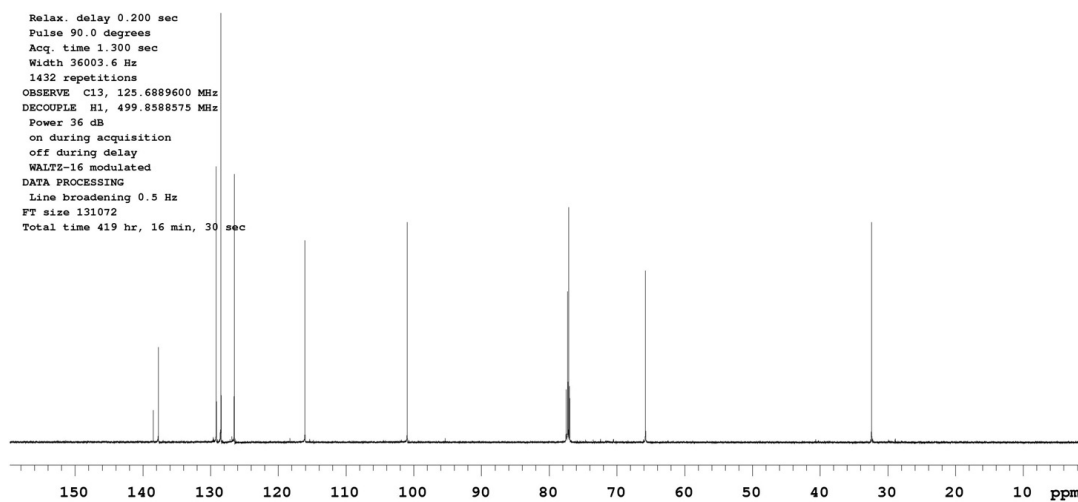
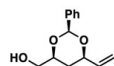
WALTZ-16 modulated

DATA PROCESSING

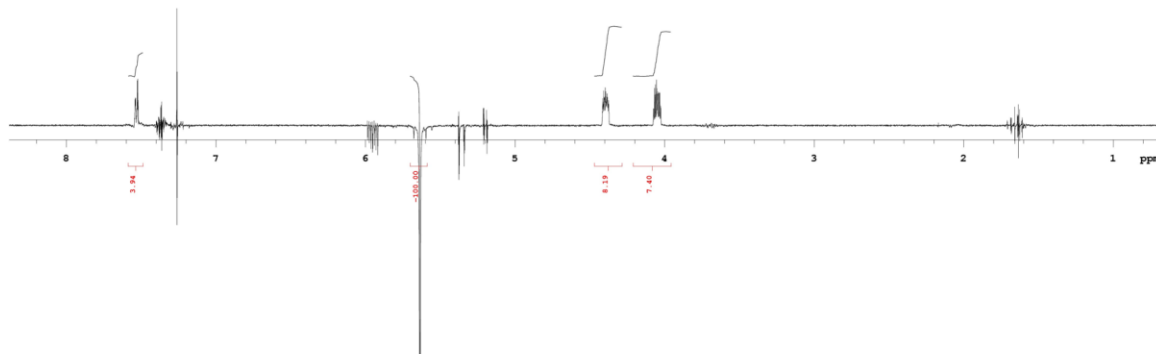
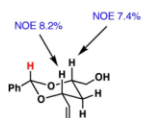
Line broadening 0.5 Hz

FT size 131072

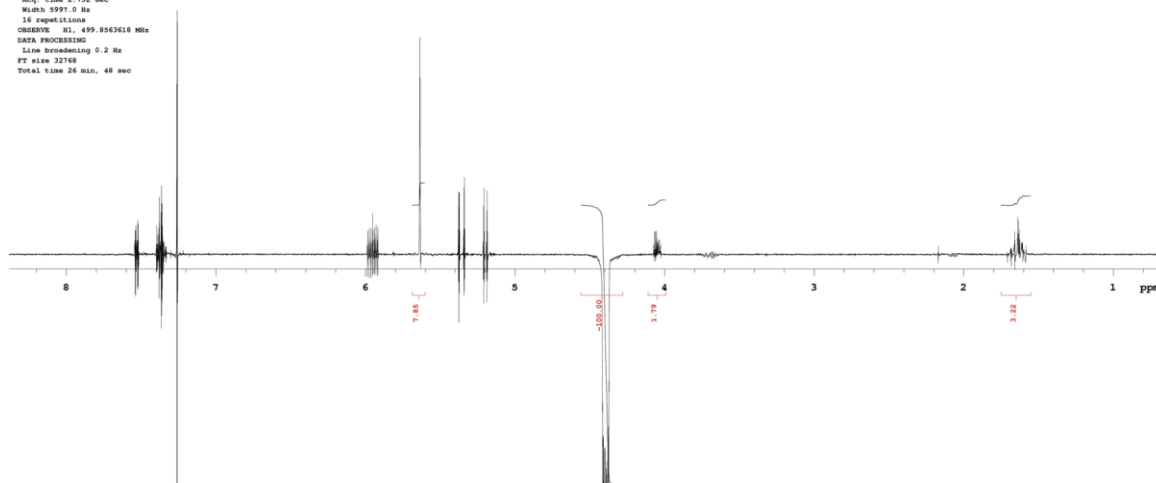
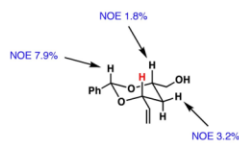
Total time 419 hr, 16 min, 30 sec



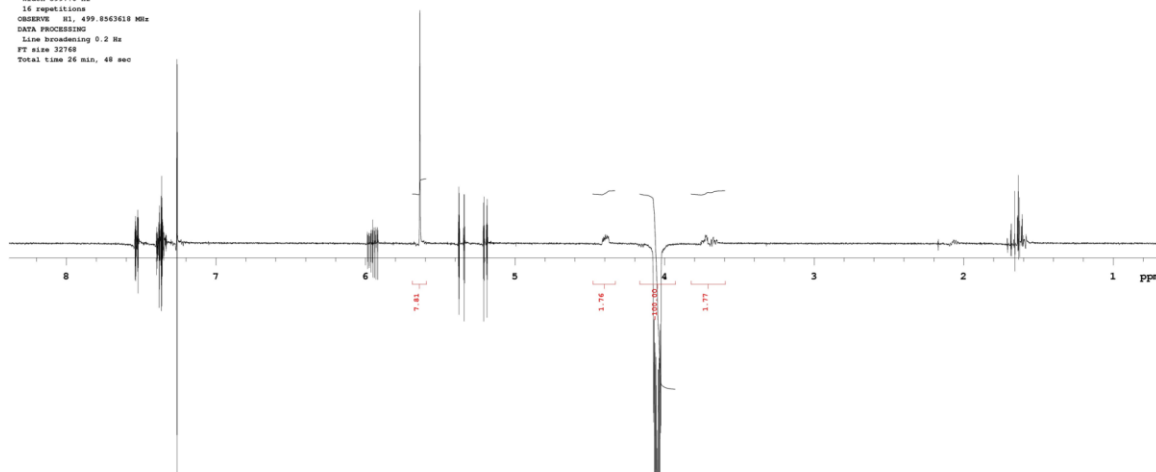
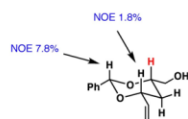
cea-5-213-nmr
 File: nmr505/Sakarian/etivala/cea-5-213-nmr.exp.fid
 Pulse Sequence: cyclopmo
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-213-nmr.exp
 INOVA-500 "nmserver"
 Relax: delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 26 min, 48 sec



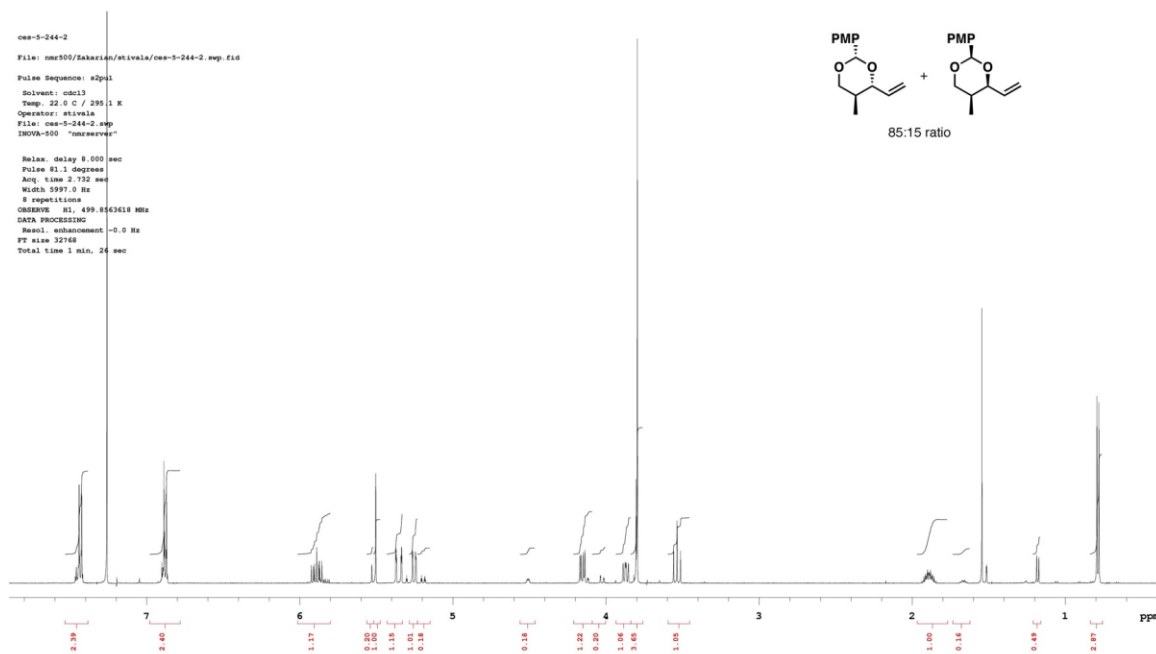
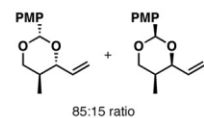
cea-5-213-nmr
 File: nmr505/Sakarian/etivala/cea-5-213-nmr.exp.fid
 Pulse Sequence: cyclopmo
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-213-nmr.exp
 INOVA-500 "nmserver"
 Relax: delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 26 min, 48 sec



cea-5-213-nmr
 File: nmr505/Sakarian/etivala/cea-5-213-nmr.exp.fid
 Pulse Sequence: cyclenoe
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-213-nmr.exp
 INOVA-500 "nmserver"
 Relax. delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8163618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 26 min, 48 sec



cea-5-244-2
 File: nmr505/Sakarian/etivala/cea-5-244-2.exp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-244-2.exp
 INOVA-500 "nmserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8163618 MHz
 DATA PROCESSING
 Resol. enhancement -0.0 Hz
 FT size 32768
 Total time 1 min, 26 sec



ces-5-244-cl3

File: nmr500/Zakarian/stivala/ces-5-244-cl3.swp.fid

Pulse Sequence: s2pul

Solvent: CDCl3

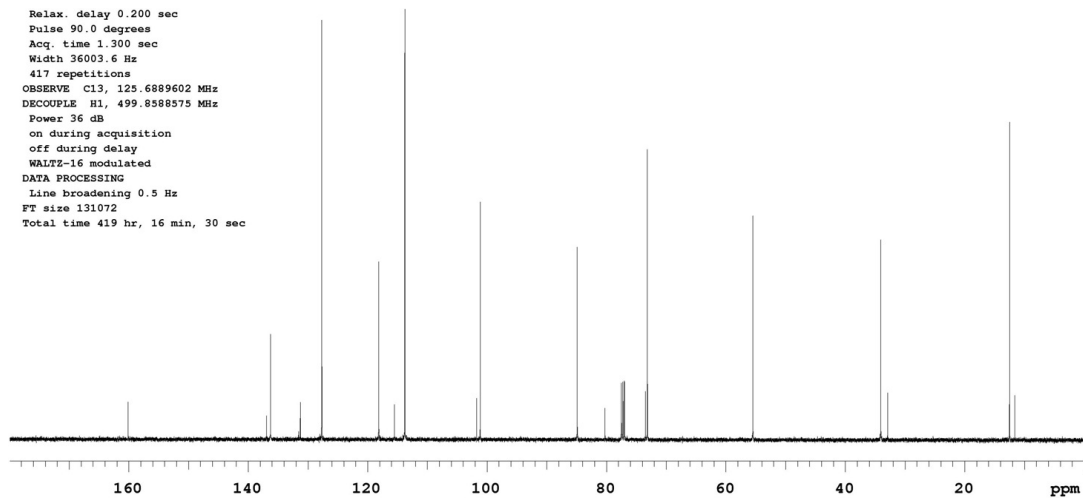
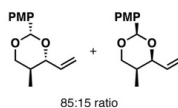
Temp. 22.0 C / 295.1 K

Operator: stivala

File: ces-5-244-cl3.swp

INOVA-500 "nmrserver"

Relax. delay 0.200 sec
Pulse 90.0 degrees
Acq. time 1.300 sec
Width 36009.6 Hz
417 repetitions
OBSERVE C13, 125.6889602 MHz
DECOUPLE H1, 499.8588575 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 419 hr, 16 min, 30 sec



ces-5-244-nov

File: nmr500/Zakarian/stivala/ces-5-244-nov.swp.fid

Pulse Sequence: cyclone

Solvent: cdcl3

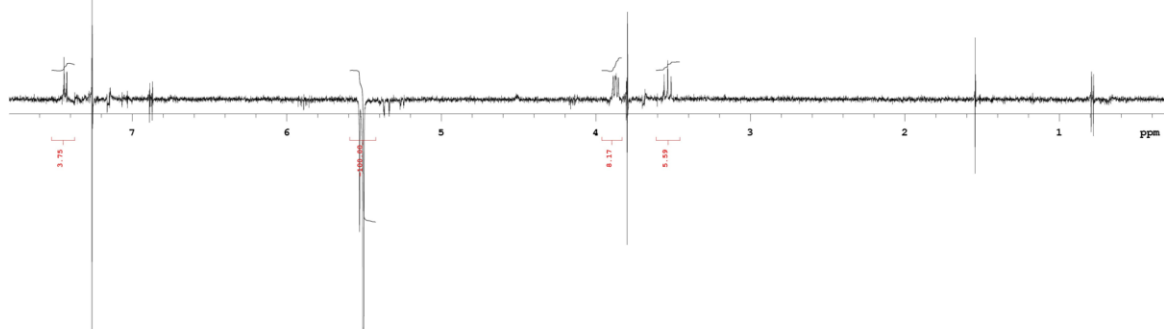
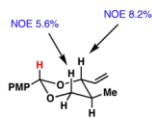
Temp. 22.0 C / 295.1 K

Operator: stivala

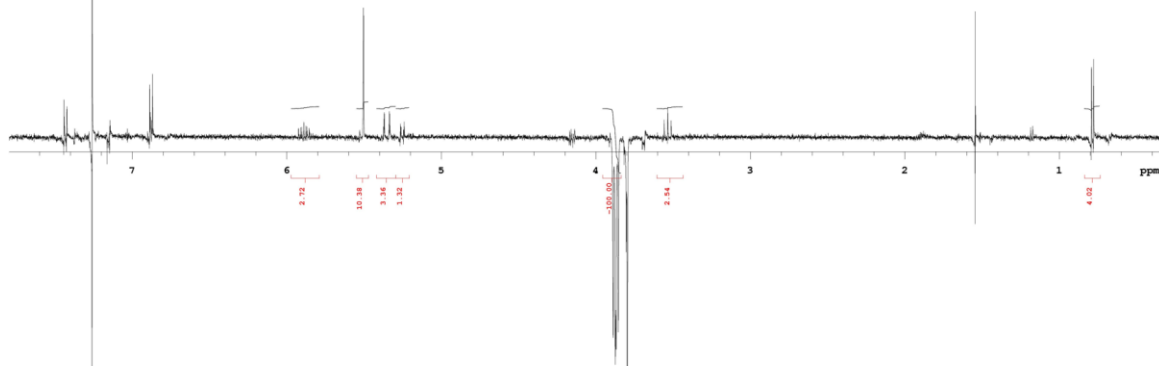
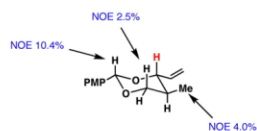
File: ces-5-244-nov.swp

INOVA-500 "nmrserver"

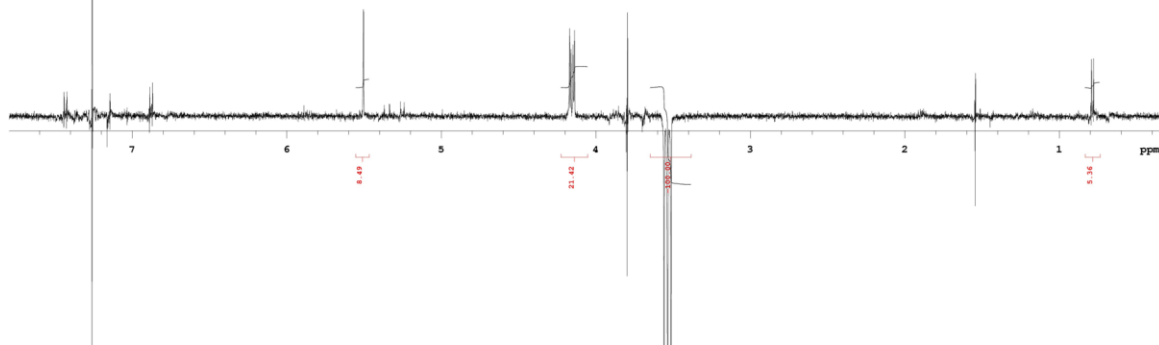
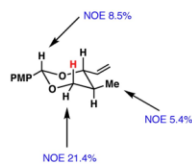
Relax. delay 10.000 sec
Pulse 91.1 degrees
Mixing 0.000 sec
Acq. time 2.732 sec
Width 5997.0 Hz
16 repetitions
OBSERVE H1, 499.8563618 MHz
DATA PROCESSING
Recal. enhancement -0.0 Hz
FT size 32768
Total time 35 min, 45 sec



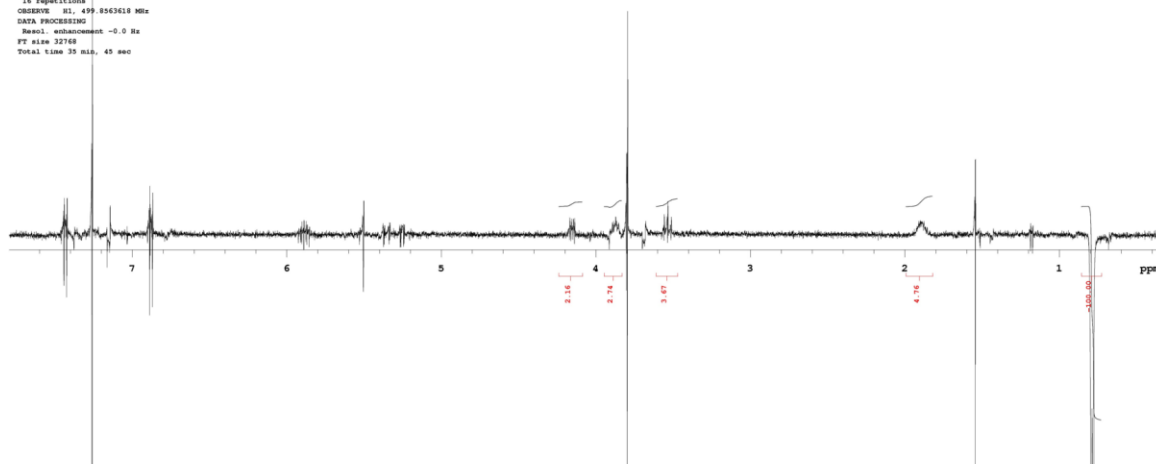
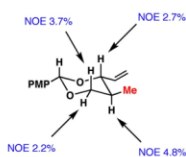
oca-5-244-nov
 File: nmr500/Sakarian/ativala/oca-5-244-nov.swp.fid
 Pulse Sequence: cyclenoe
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: ativala
 File: oca-5-244-nov.swp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Recal. enhancement -0.0 Hz
 FT size 32768
 Total time 35 min, 45 sec



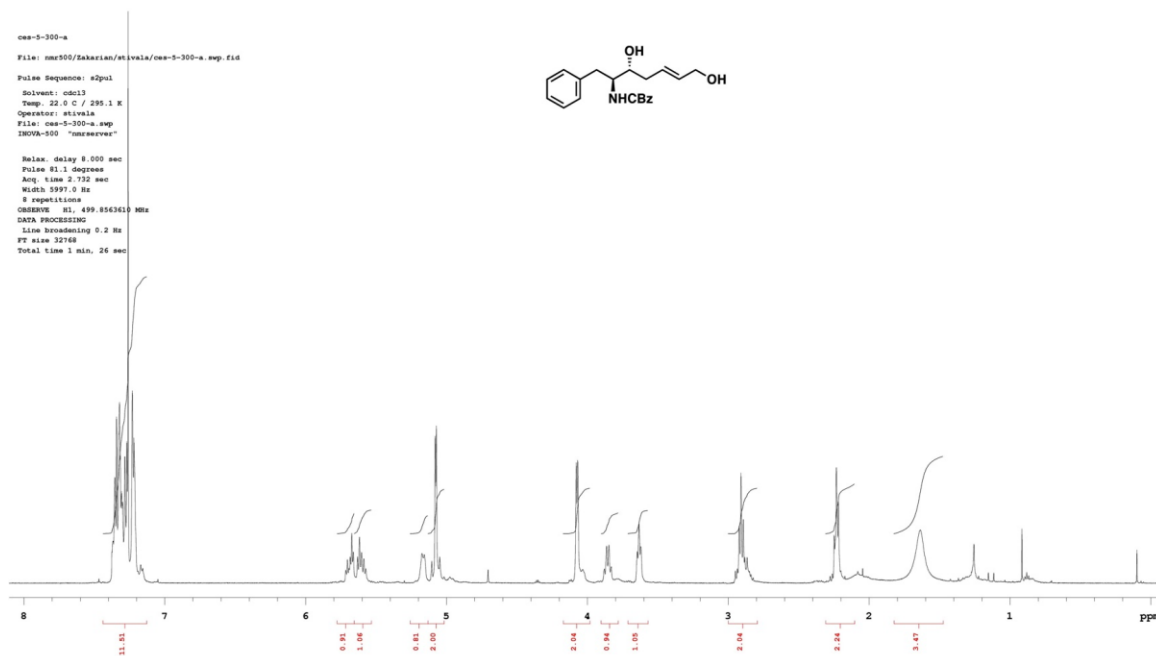
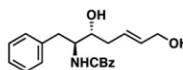
oca-5-244-nov
 File: nmr500/Sakarian/ativala/oca-5-244-nov.swp.fid
 Pulse Sequence: cyclenoe
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: ativala
 File: oca-5-244-nov.swp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Recal. enhancement -0.0 Hz
 FT size 32768
 Total time 35 min, 45 sec



cea-5-244-nov
 File: nmr500/Sakarian/etivala/cea-5-244-nov.swp.fid
 Pulse Sequence: cyclohexa
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-244-nov.swp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Recal. enhancement -0.0 Hz
 FT size 32768
 Total time 35 min, 45 sec



cea-5-300-a
 File: nmr500/Sakarian/etivala/cea-5-300-a.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: etivala
 File: cea-5-300-a.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line Broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



ces-5-300-a-c13

File: nmr500/Zakarian/stivala/ces-5-300-a-c13.swp.fid

Pulse Sequence: s2pul

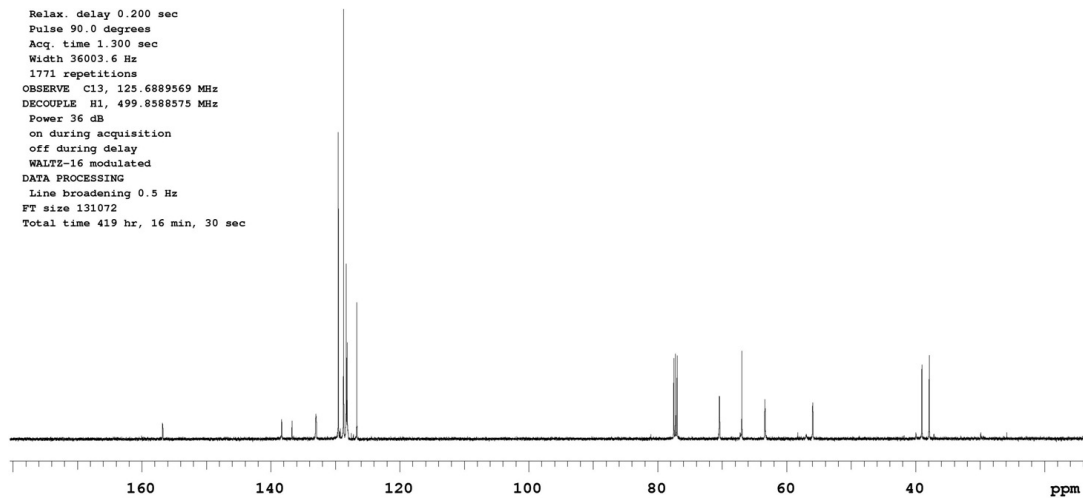
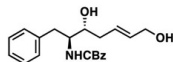
Solvent: CDCl3

Temp. 22.0 C / 295.1 K

Operator: stivala

File: ces-5-300-a-c13.swp

INOVA-500 "nmrserver"



ces-6-16-2

File: nmr500/Zakarian/stivala/ces-6-16-2.swp.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp. 22.0 C / 295.1 K

Operator: stivala

File: ces-6-16-2.swp

INOVA-500 "nmrserver"

Relax. delay 8.000 sec

Pulse 91.1 degrees

Acq. time 2.730 sec

Width 5997.0 Hz

8 repetitions

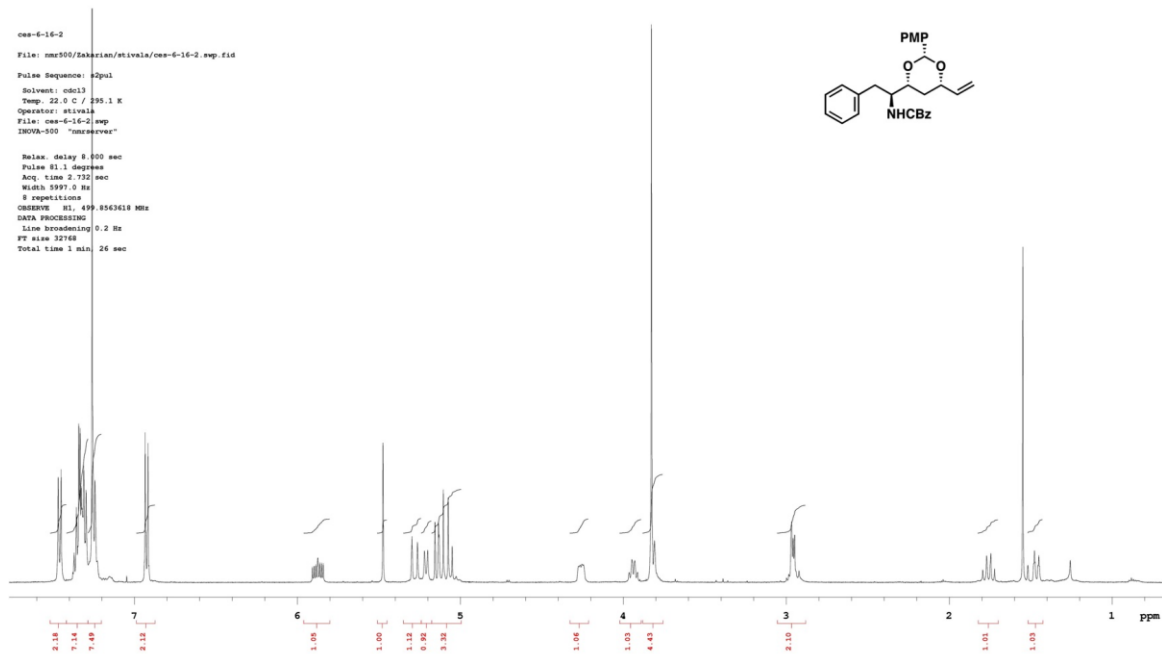
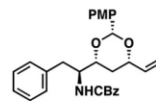
OBSERVE H1, 499.8563619 MHz

DATA PROCESSING

Line broadening 0.2 Hz

FT size 32768

Total time 1 min, 26 sec

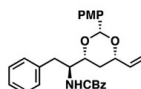


ces-6-16-cl3

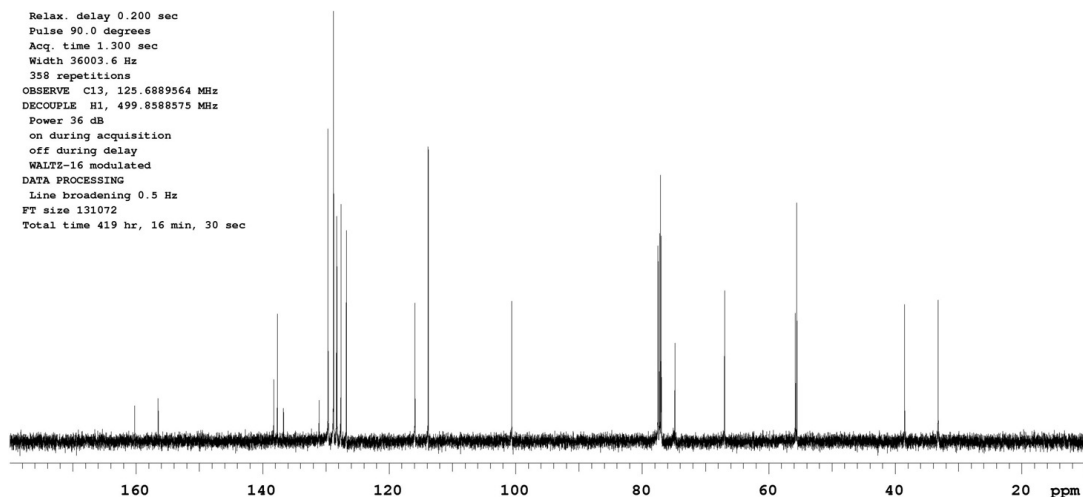
File: nmr500/Zakarian/stivala/ces-6-16-cl3.swp.fid

Pulse Sequence: s2pul

Solvent: CDCl3
Temp. 22.0 C / 295.1 K
Operator: stivala
File: ces-6-16-cl3.swp
INOVA-500 "nmrserver"



Relax. delay 0.200 sec
Pulse 90.0 degrees
Acq. time 1.300 sec
Width 36003.6 Hz
358 repetitions
OBSERVE Cl3, 125.6889564 MHz
DECOUPLE H1, 499.8588575 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 419 hr, 16 min, 30 sec

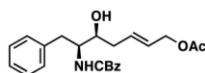


ath-1-034-repurified-1H

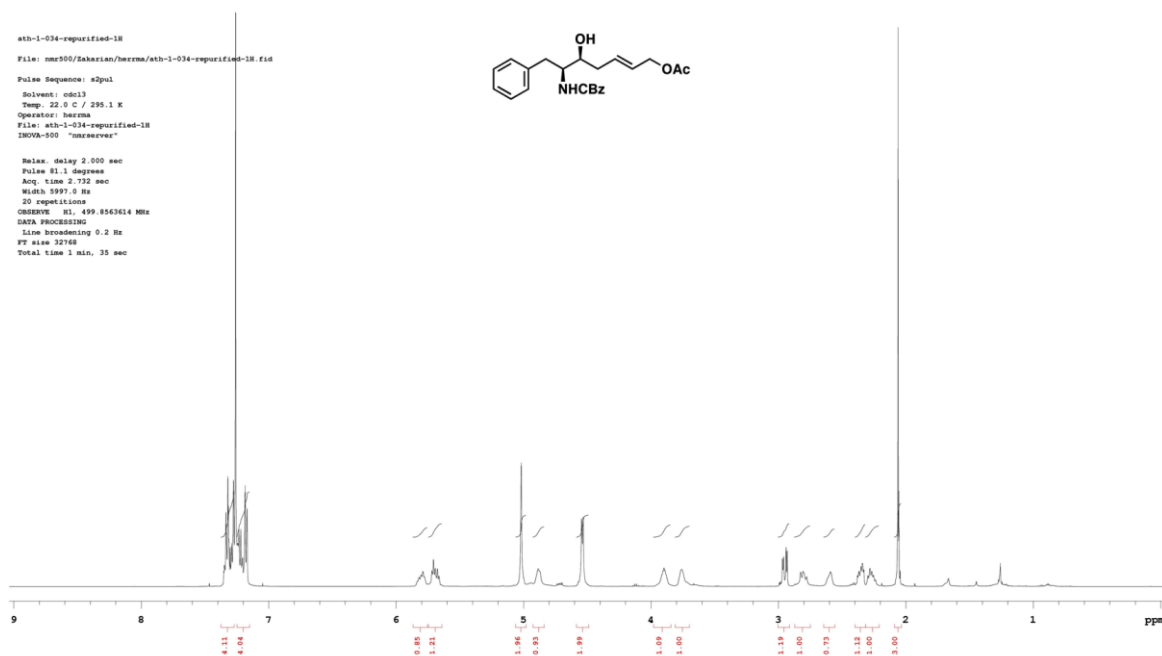
File: nmr500/Zakarian/berma/ath-1-034-repurified-1H.fid


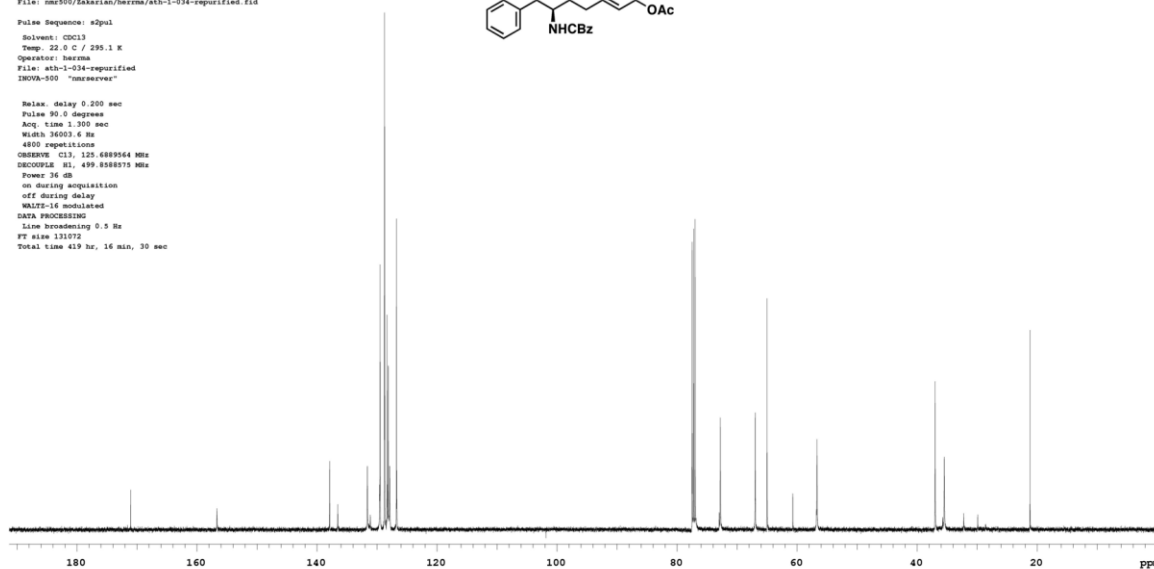
Pulse Sequence: s2pul

Solvent: cdcl3
Temp. 22.0 C / 295.1 K
Operator: berma
File: ath-1-034-repurified-1H
INOVA-500 "nmrserver"

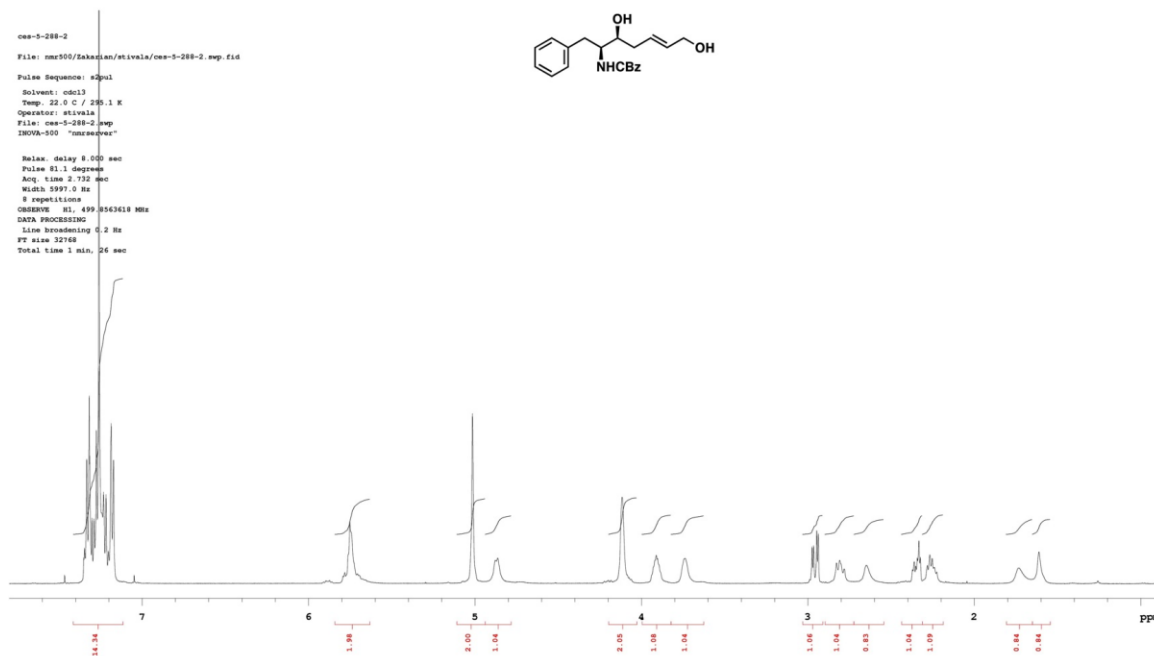


Relax. delay 2.000 sec
Pulse 91.1 degrees
Acq. time 0.732 sec
Width 5997.0 Hz
20 repetitions
OBSERVE H1, 499.8543614 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 35 sec



CCOC(=O)/C=C/C[C@H](O)[C@@H](NC(=O)c1ccccc1)Cc2ccccc2

Chemical structure of (S)-1-benzyl-4-hydroxy-5-phenylpent-2-en-3-ol, showing a benzyl group, a chiral center with an NHCBz group, and a terminal hydroxyl group.



ces-5-288-cl3-mcoh

File: nmz500/Zakarian/stivala/ces-5-288-cl3-mcoh.swp.fid

Pulse Sequence: s2pul

Solvent: CDC13

Temp. 22.0 C / 295.1 K

Operator: stivala

File: ces-5-288-cl3-mcoh.swp

INOVA-500 "nmrserver"

Relax. delay 0.200 sec

Pulse 90.0 degrees

Acq. time 1.300 sec

Width 36003.6 Hz

2283 repetitions

OBSERVE C13, 125.6892796 MHz

DECOUPLE H1, 499.8588575 MHz

Power 36 dB

on during acquisition

off during delay

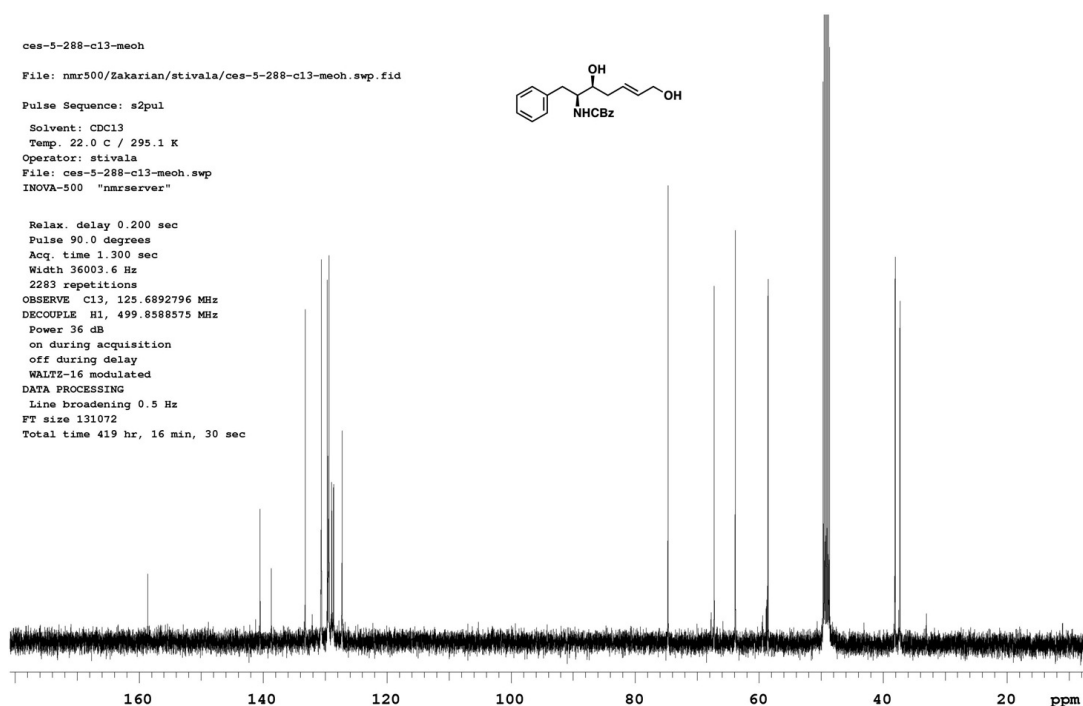
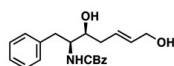
WALTZ-16 modulated

DATA PROCESSING

Line broadening 0.5 Hz

FT size 131072

Total time 419 hr, 16 min, 30 sec



ces-5-292-3

File: nmz500/Zakarian/stivala/ces-5-292-3.swp.fid

Pulse Sequence: s2pul

Solvent: cdcl3

Temp. 22.0 C / 295.1 K

Operator: stivala

File: ces-5-292-3.swp

INOVA-500 "nmrserver"

Relax. delay 1.000 sec

Pulse 61.1 degrees

Acq. time 0.732 sec

Width 5997.0 Hz

Single scan

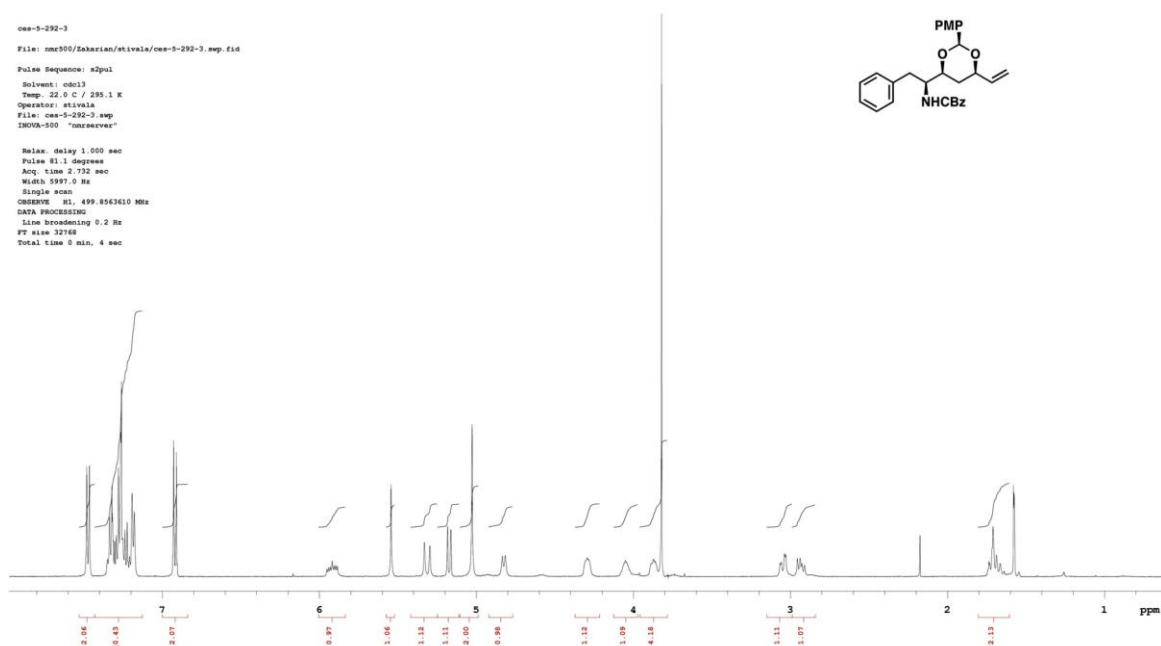
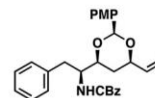
OBSERVE H1, 499.8563610 MHz

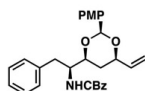
DATA PROCESSING

Line broadening 0.2 Hz

FT size 32768

Total time 0 min, 4 sec

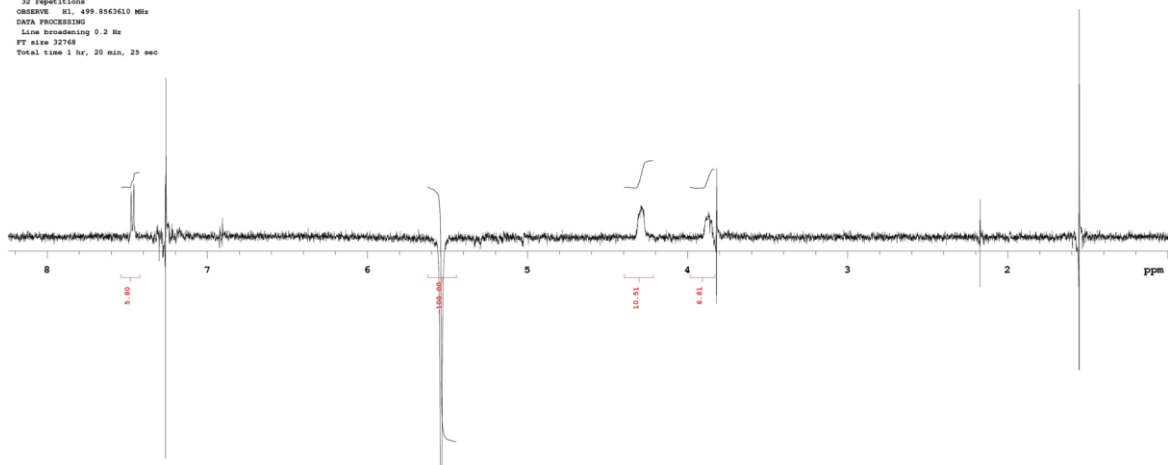
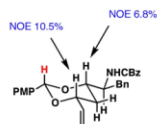
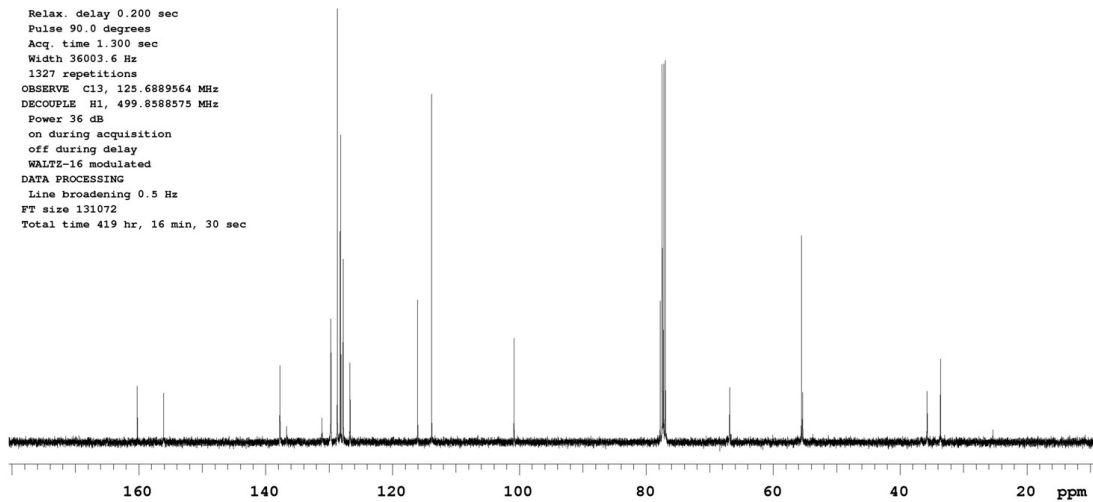




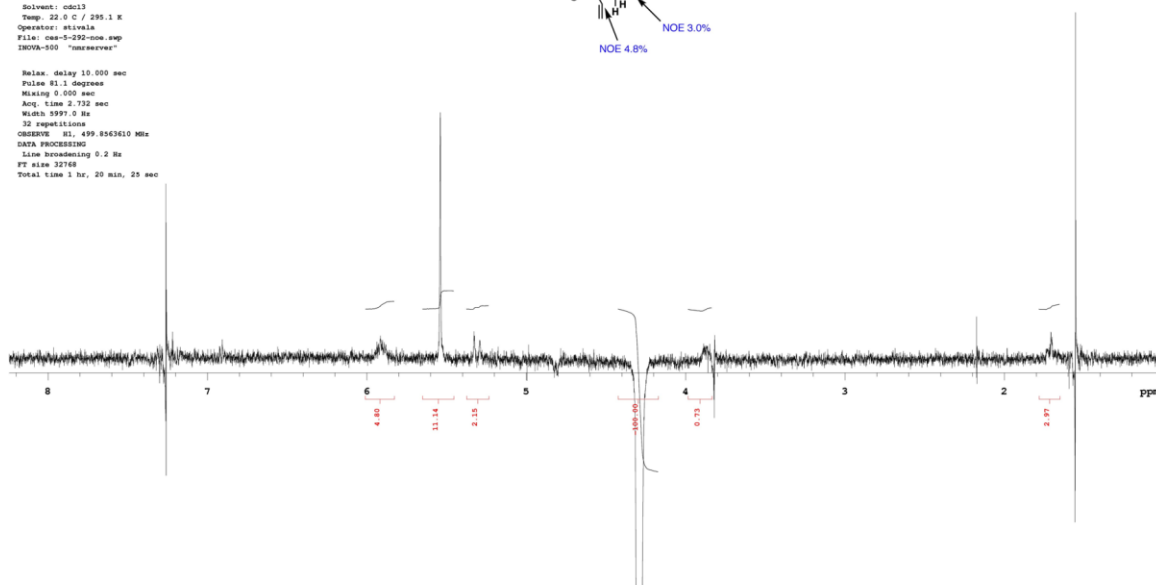
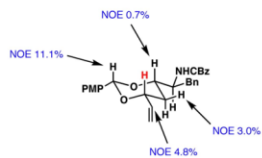
```

Relax. delay 0.200 sec
Pulse 90.0 degrees
Acq. time 1.300 sec
Width 36003.6 Hz
1327 repetitions
OBSERVE C13, 125.62889564 MHz
DECOUPLE H1, 499.8588575 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 419 hr, 16 min, 30 sec

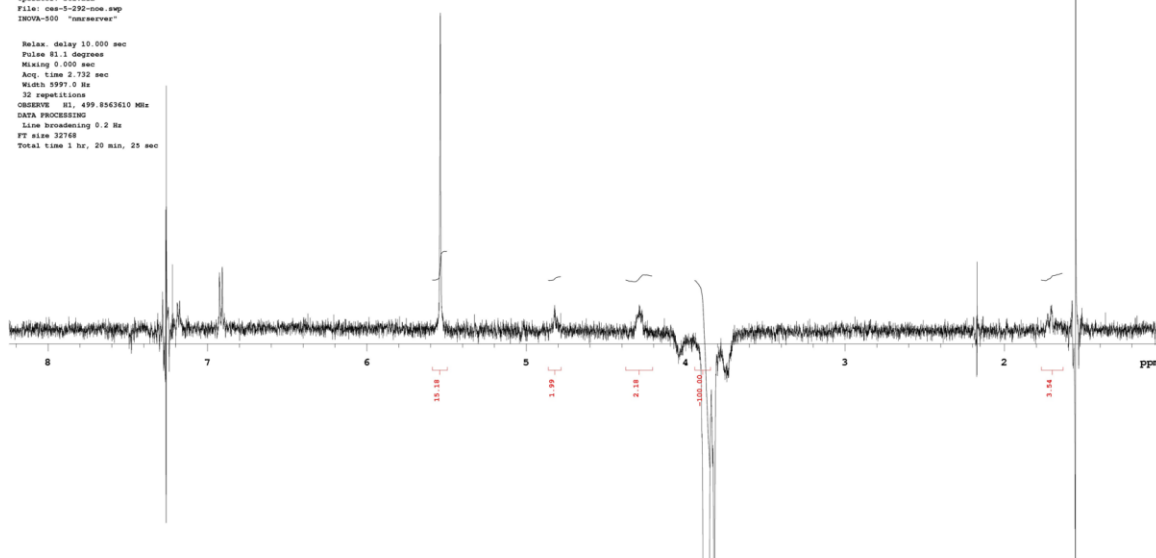
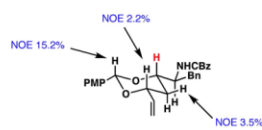
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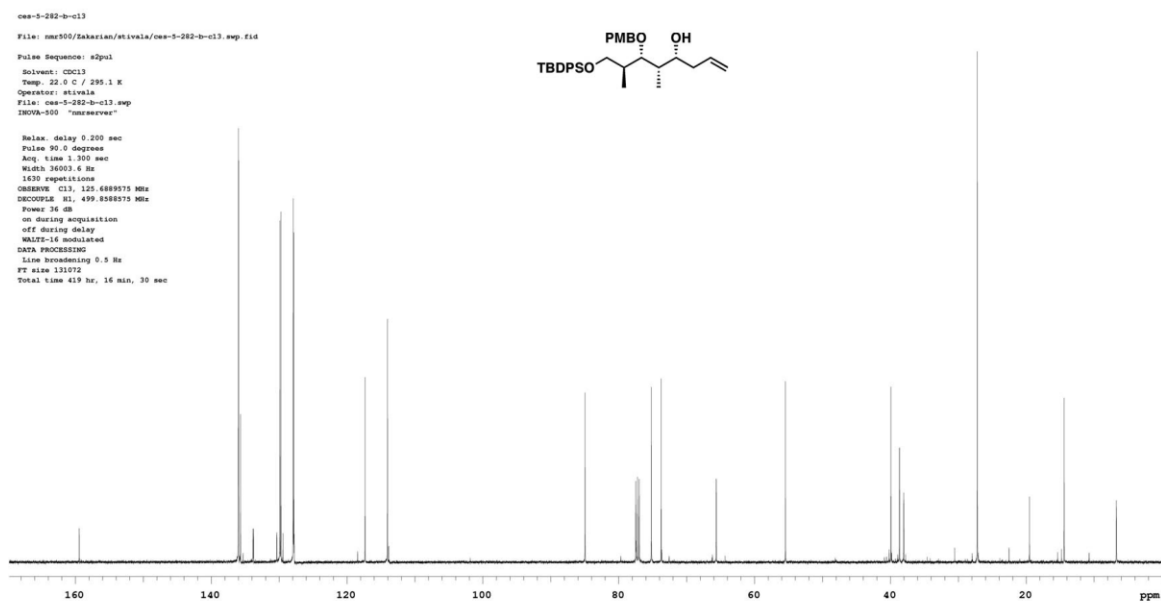
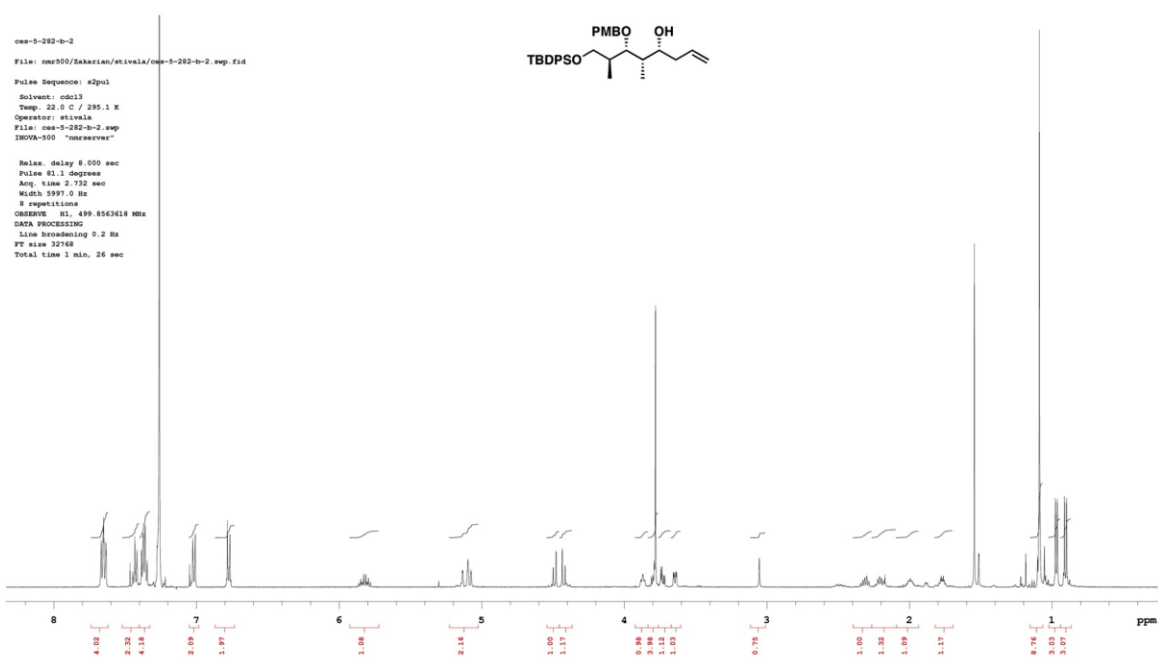


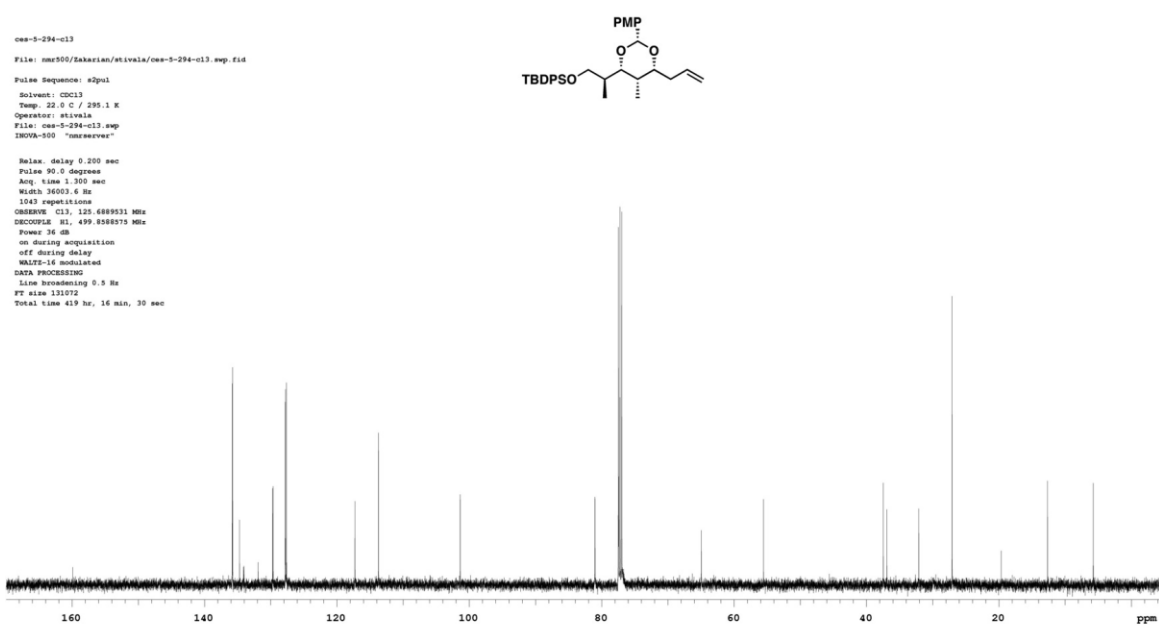
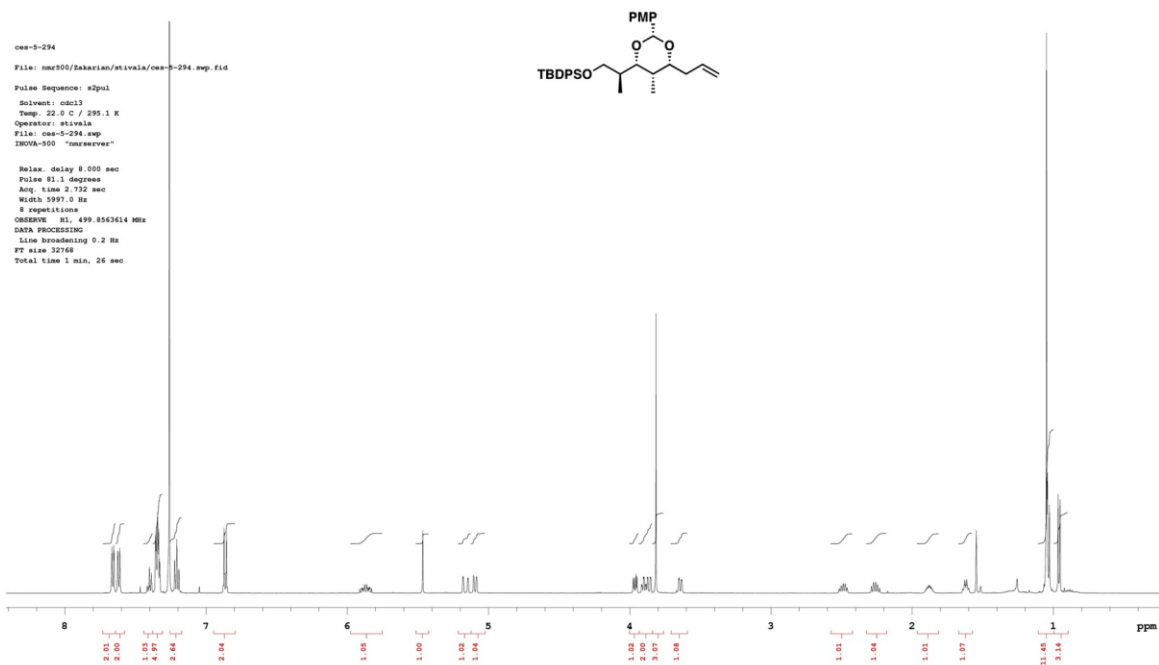
ces-3-292-noe
 File: nmr505/Ekharian/Alivis/ces-3-292-noe.swp.fid
 Pulse Sequence: zgpg30
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: Alivis
 File: ces-3-292-noe.swp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse #1.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 32 repetitions
 OBSERVE R1, 499.8563610 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 hr, 20 min, 25 sec



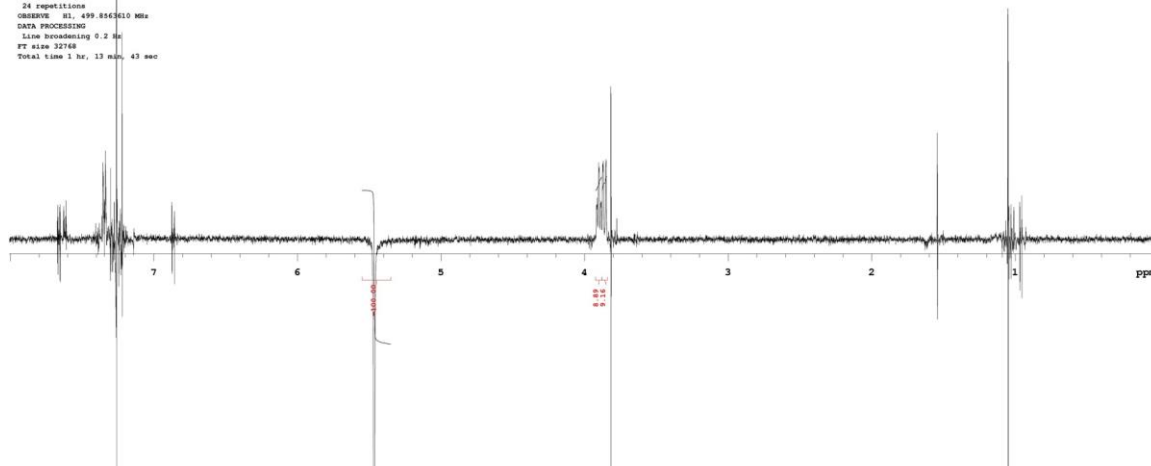
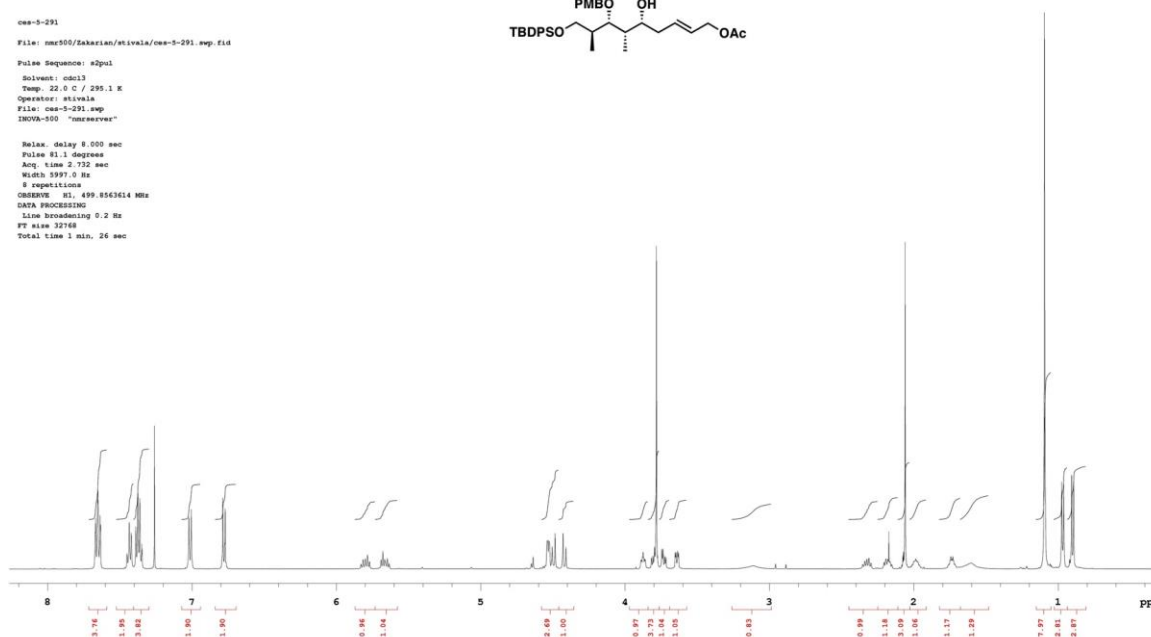
ces-3-292-noe
 File: nmr505/Ekharian/Alivis/ces-3-292-noe.swp.fid
 Pulse Sequence: zgpg30
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: Alivis
 File: ces-3-292-noe.swp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse #1.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 32 repetitions
 OBSERVE R1, 499.8563610 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 hr, 20 min, 25 sec



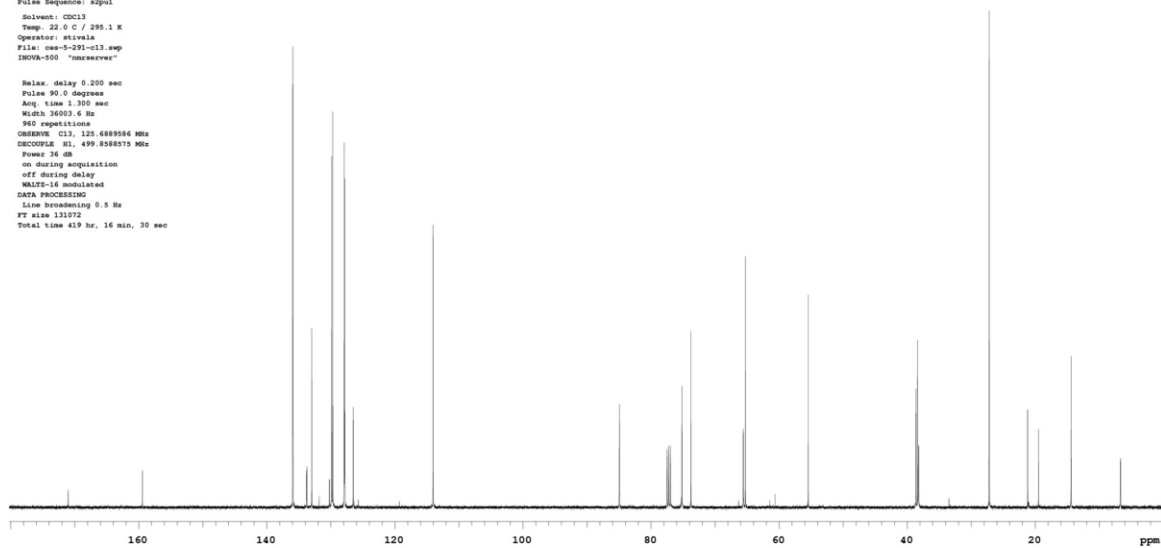
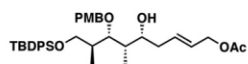




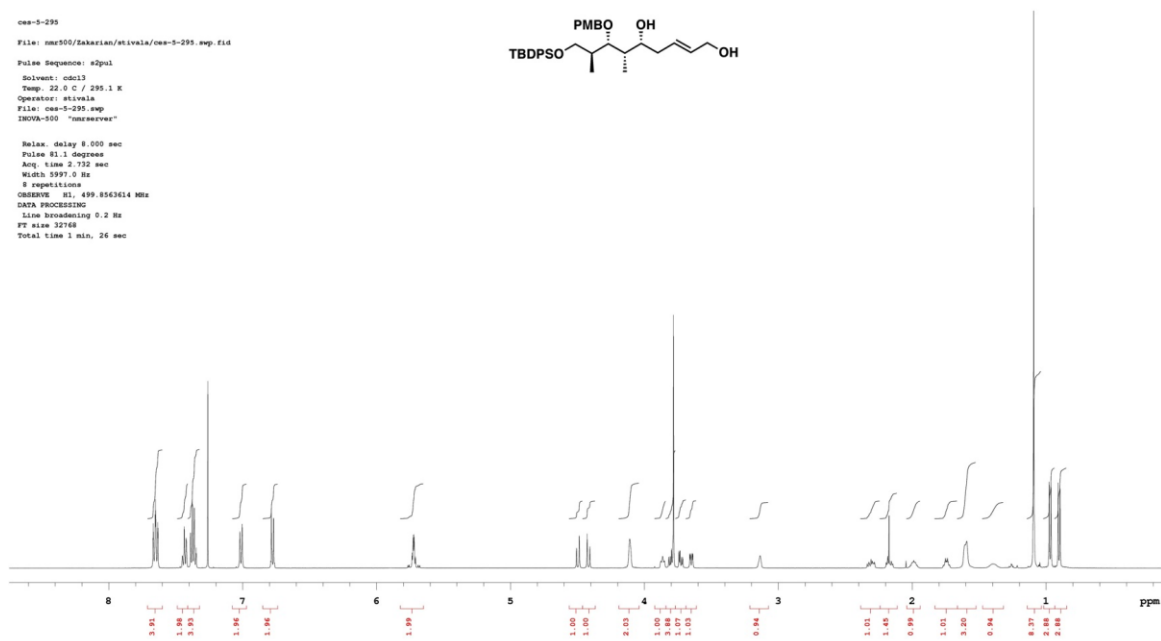
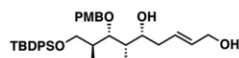
Chemical structure of compound 10, a bicyclic molecule with a PMP group and a TBDPSO group. Two NOE correlations are indicated: NOE 9.2% between the PMP group and a proton, and NOE 8.9% between the TBDPSO group and a proton.

CCOC(=O)/C=C/[C@H](O)[C@H](COP(=O)(OC)OC)[C@H](C)OP(=O)(OC)OC

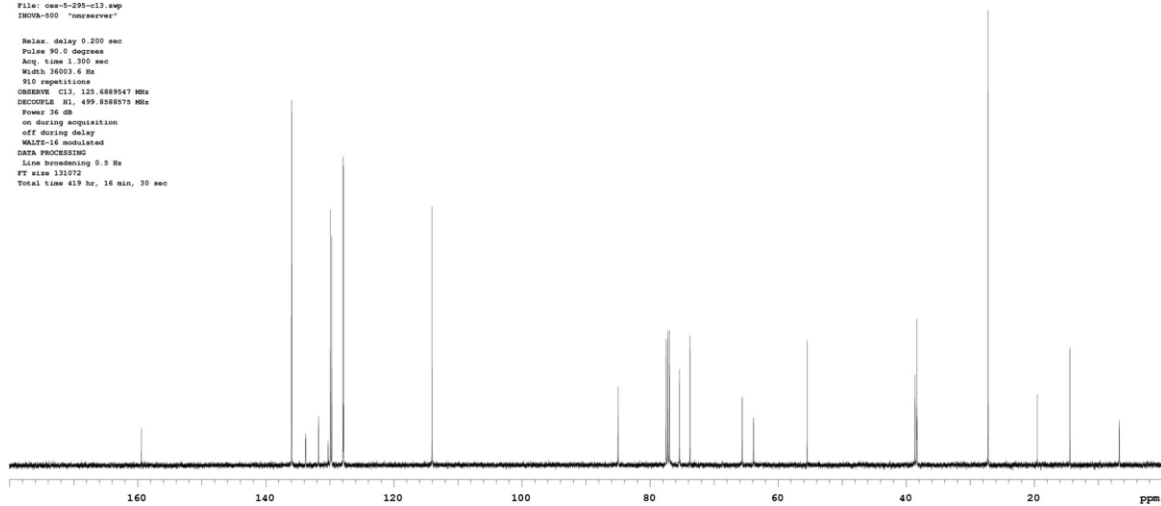
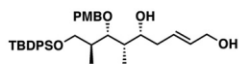
cas-5-291-c13
 File: nmr505/Eakarian/stivaia/cas-5-291-c13.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-5-291-c13.swp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 960 repetitions
 OBSERVE C13, 125.689556 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



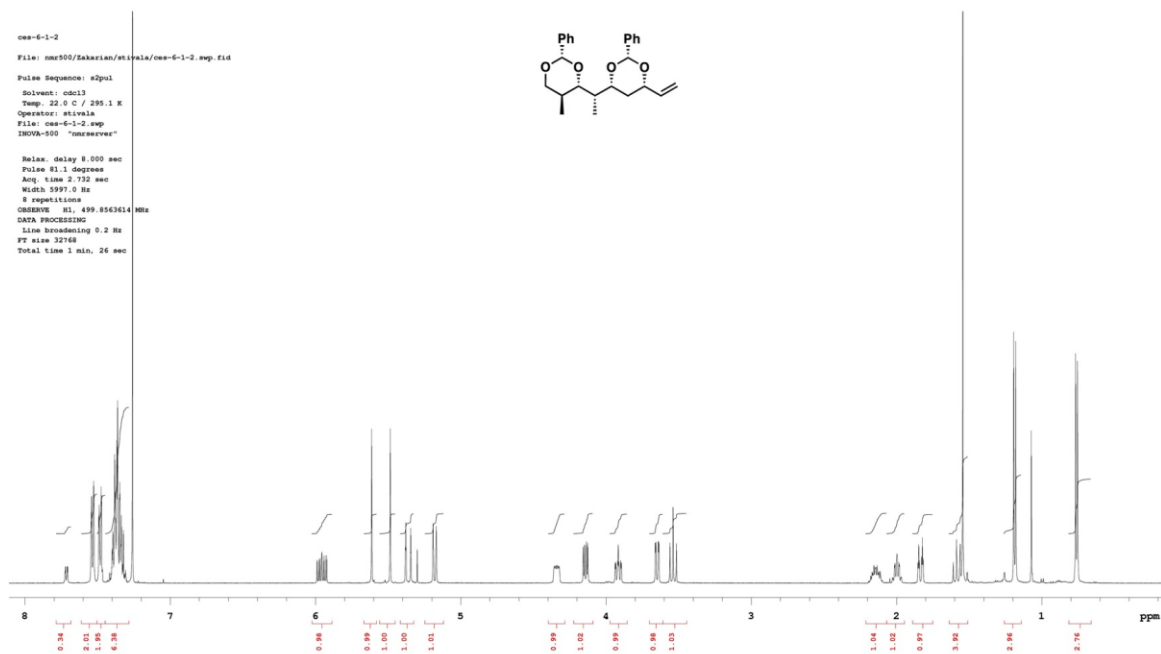
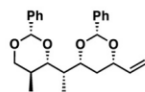
cas-5-295
 File: nmr505/Eakarian/stivaia/cas-5-295.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-5-295.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



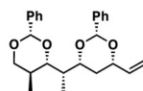
cas-5-295-c13
 File: nmr500/Eakarian/stivaia/cas-5-295-c13.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-5-295-c13.swp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 910 repetitions
 OBSERVE CH1, 120.688547 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



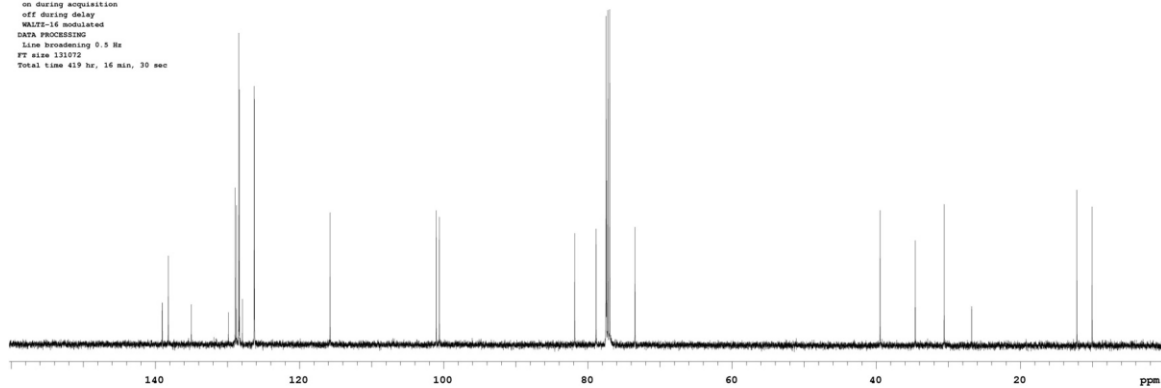
cas-6-1-2
 File: nmr500/Eakarian/stivaia/cas-6-1-2.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-6-1-2.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



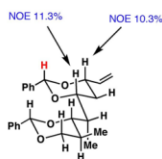
ces-6-1-c13
 File: nmr500/Ekharian/stivala/ces-6-1-c13.exp.fid
 Pulse Sequence: zgpg30
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivala
 File: ces-6-1-c13.exp
 INOVA-500 "nmrserver"



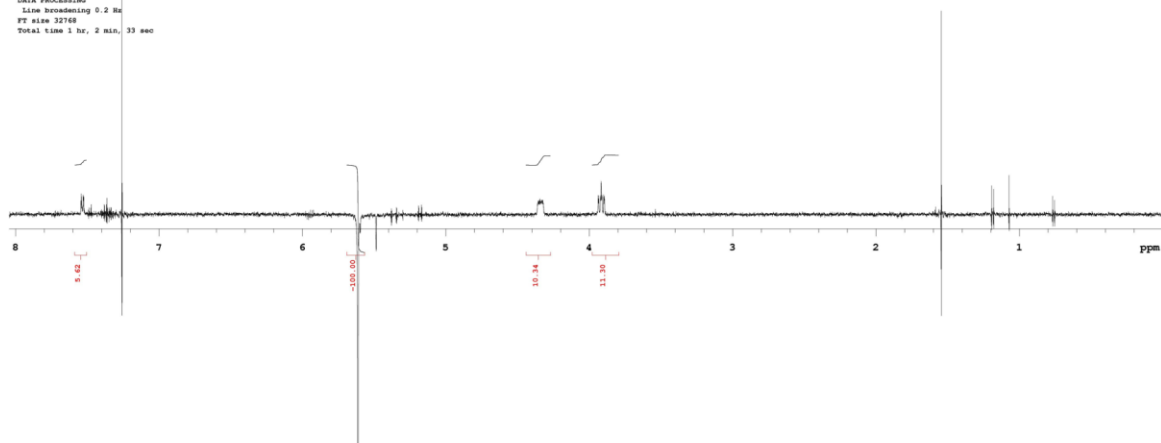
Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 1425 repetitions
 OBSERVE CH, 125.688547 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



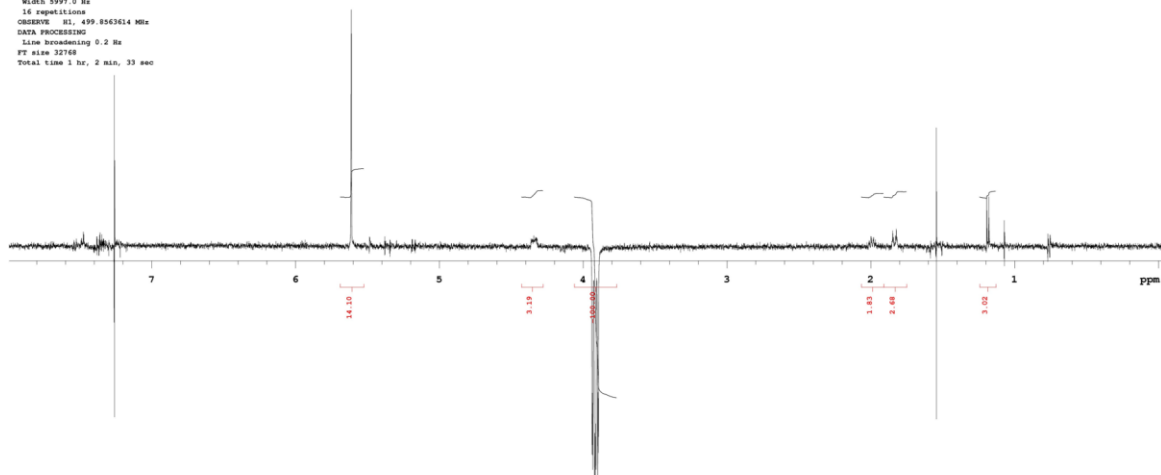
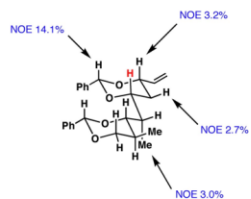
ces-6-1-noe
 File: nmr500/Ekharian/stivala/ces-6-1-noe.fid
 Pulse Sequence: zgpg30
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivala
 File: ces-6-1-noe
 INOVA-500 "nmrserver"



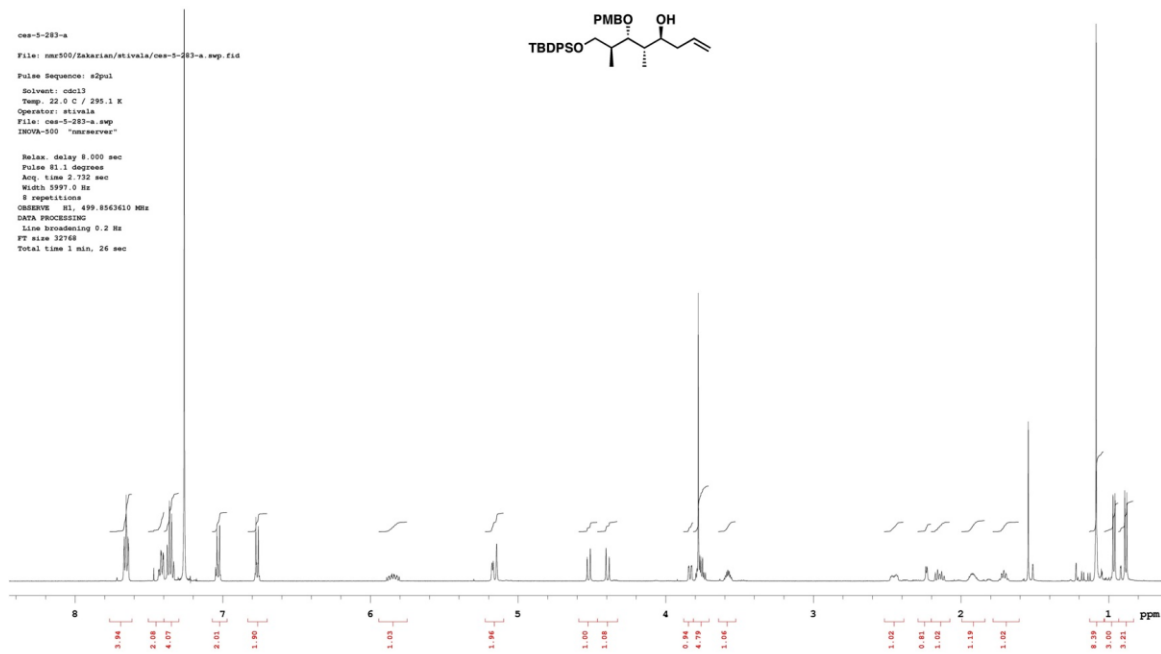
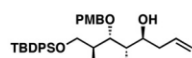
Relax. delay 10.000 sec
 Pulse 91.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 hr, 2 min, 33 sec



ces-6-1-noe
 File: nmr500/Ekharian/stilvala/ces-6-1-noe.fid
 Pulse Sequence: zgpg30
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stilvala
 File: ces-6-1-noe
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse 61.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE R1 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 hr, 2 min, 33 sec



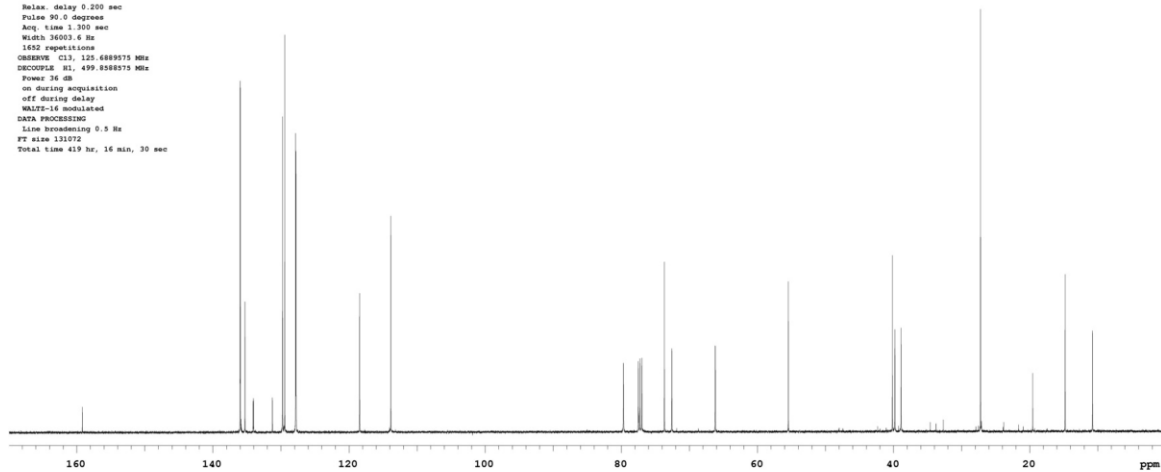
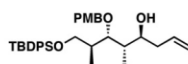
ces-5-283-a
 File: nmr500/Ekharian/stilvala/ces-5-283-a.exp.fid
 Pulse Sequence: zgpg30
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stilvala
 File: ces-5-283-a.exp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 61.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE R1 499.8563610 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



cas-5-282-a-c13
File: nmr500/Ekharian/stivala/cas-5-282-a-c13.swp.fid

Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 22.0 C / 295.1 K
Operator: stivala
File: cas-5-282-a-c13.swp
INOVA-500 "nmzserver"

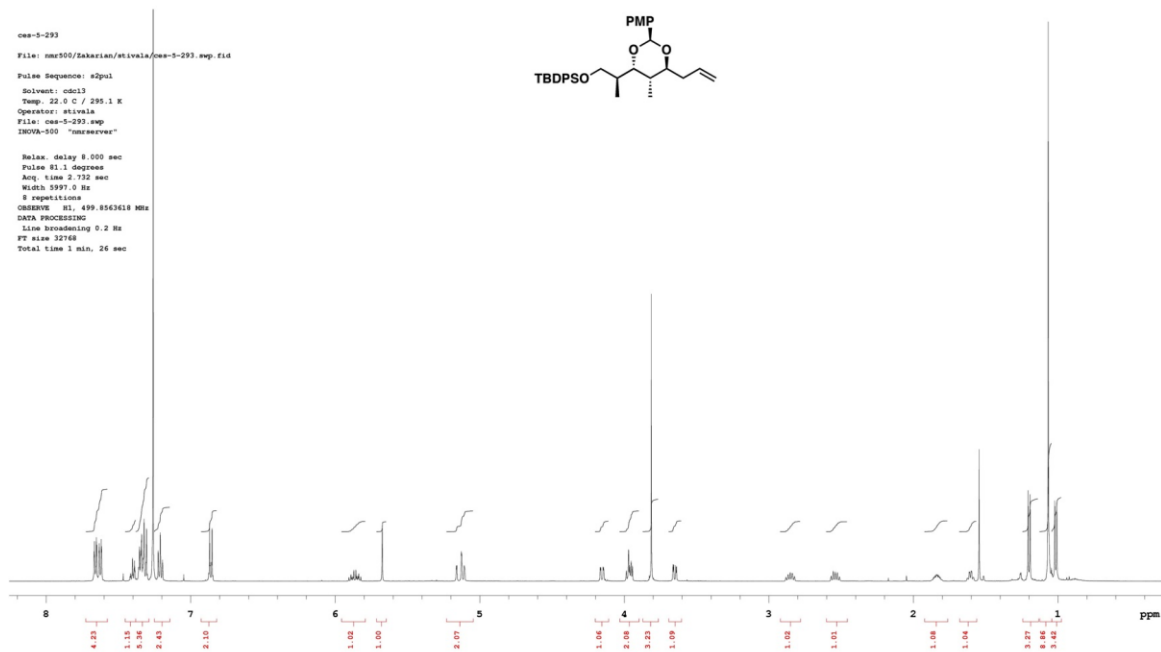
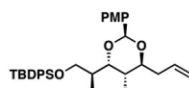
Relax. delay 0.200 sec
Pulse 90.0 degrees
Acq. time 1.300 sec
Width 36003.6 Hz
1452 repetitions
GHSBNS c13, 125.6889575 MHz
DECOUPLE H1, 499.8588575 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 121072
Total time 419 hr, 16 min, 30 sec

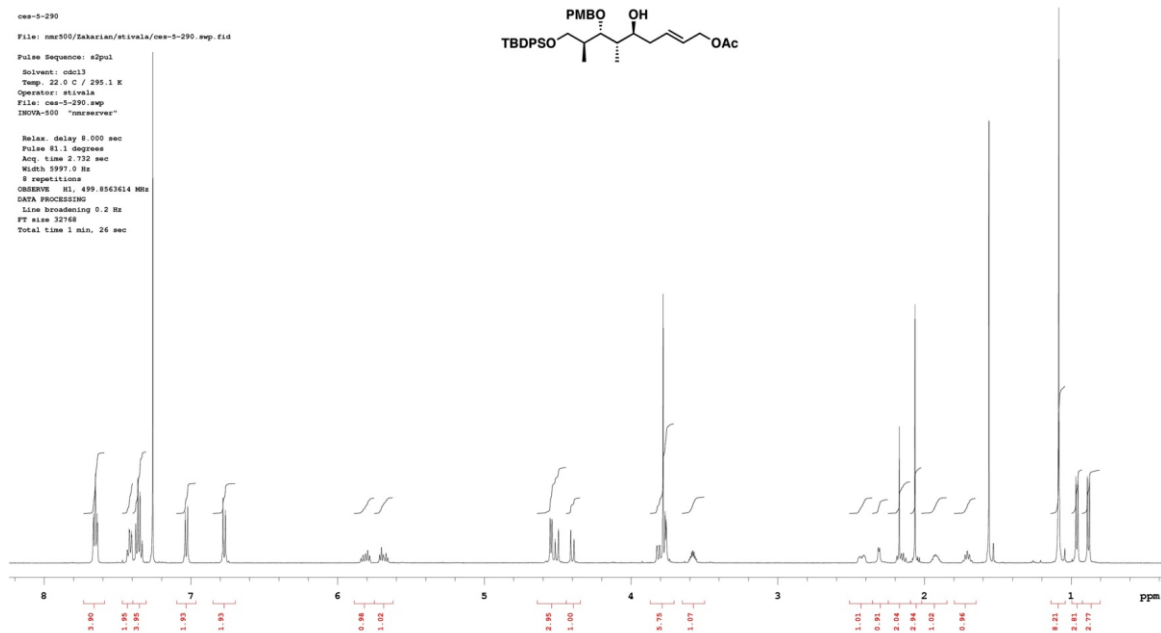
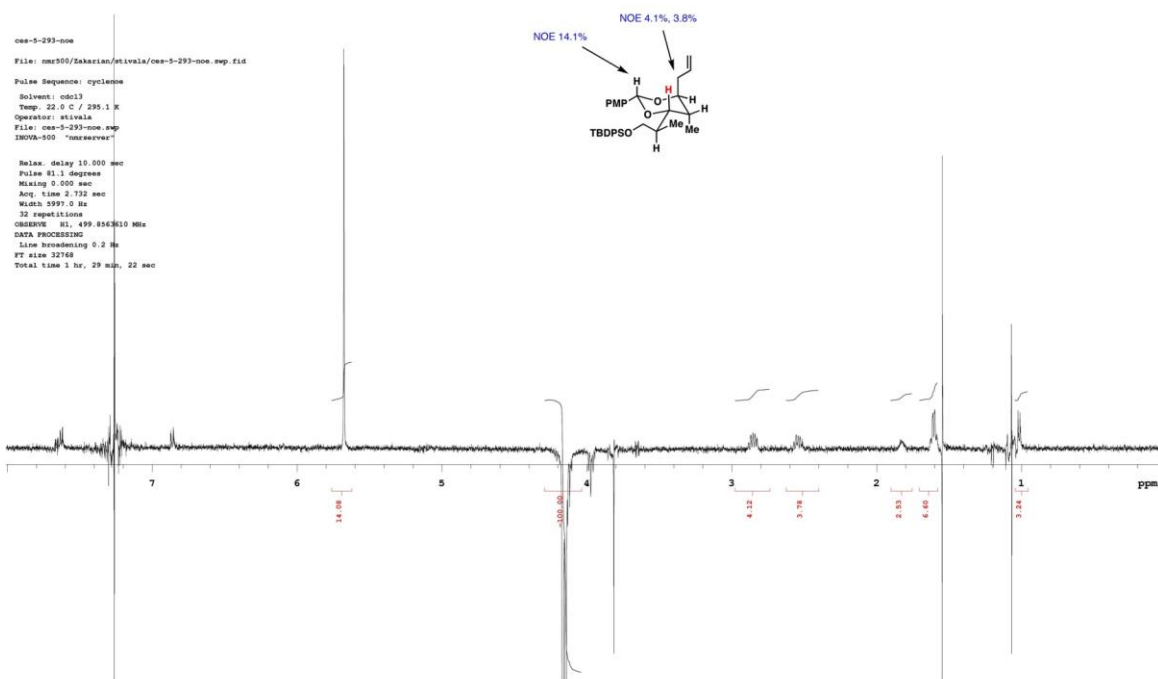


cas-5-293
File: nmr500/Ekharian/stivala/cas-5-293.swp.fid

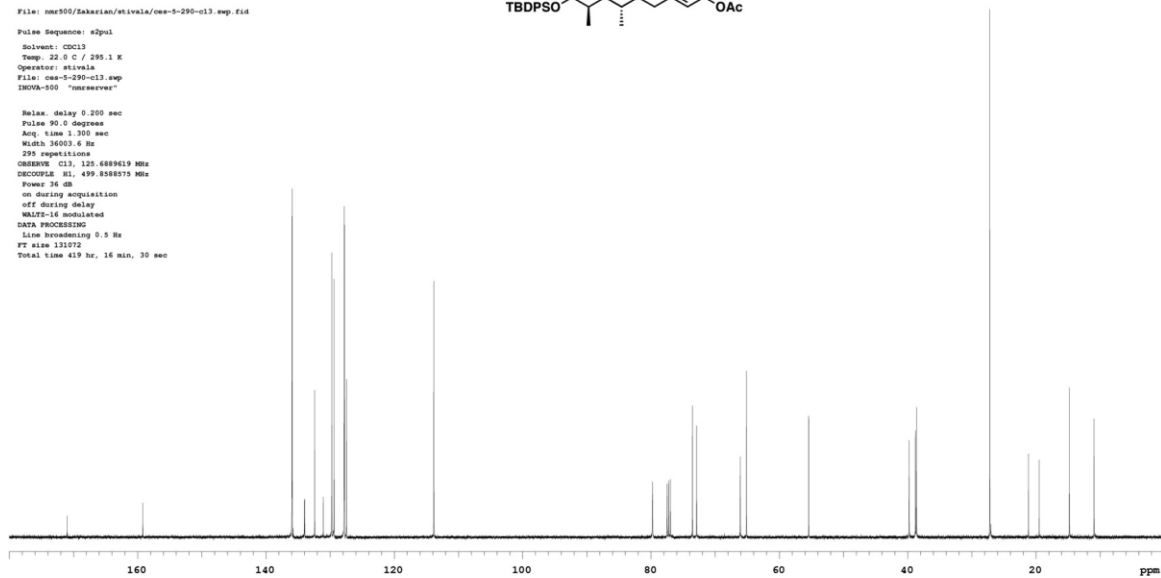
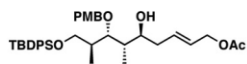
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 22.0 C / 295.1 K
Operator: stivala
File: cas-5-293.swp
INOVA-500 "nmzserver"

Relax. delay 8.000 sec
Pulse 81.1 degrees
Acq. time 2.732 sec
Width 5997.0 Hz
8 repetitions
GHSBNS H1, 499.8563618 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 26 sec

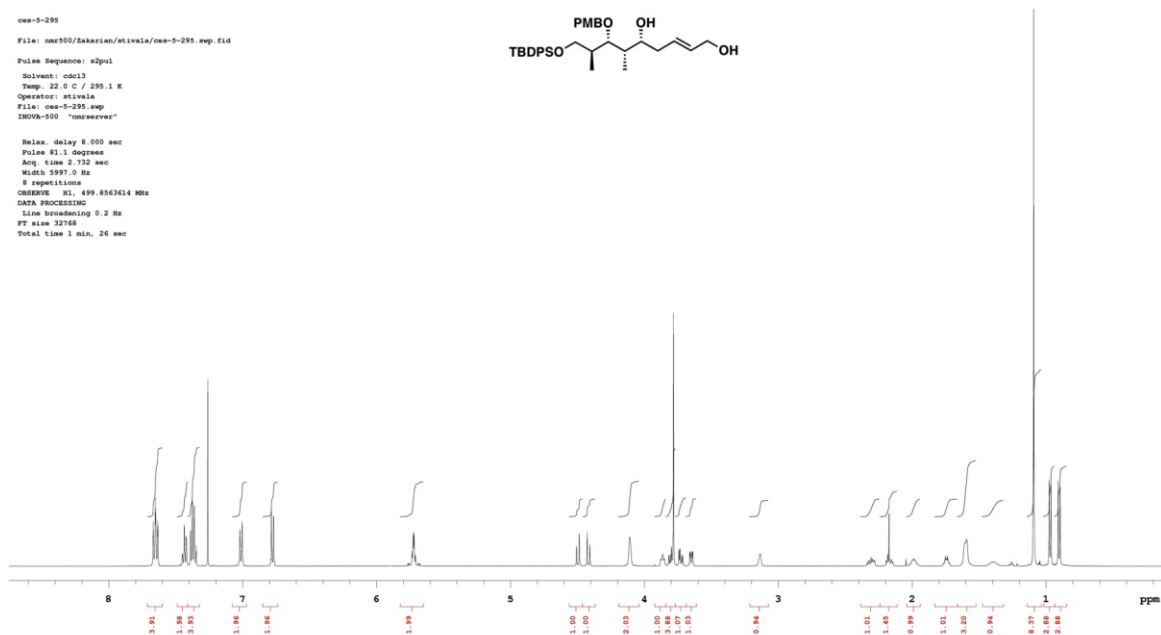
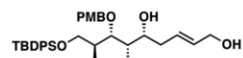




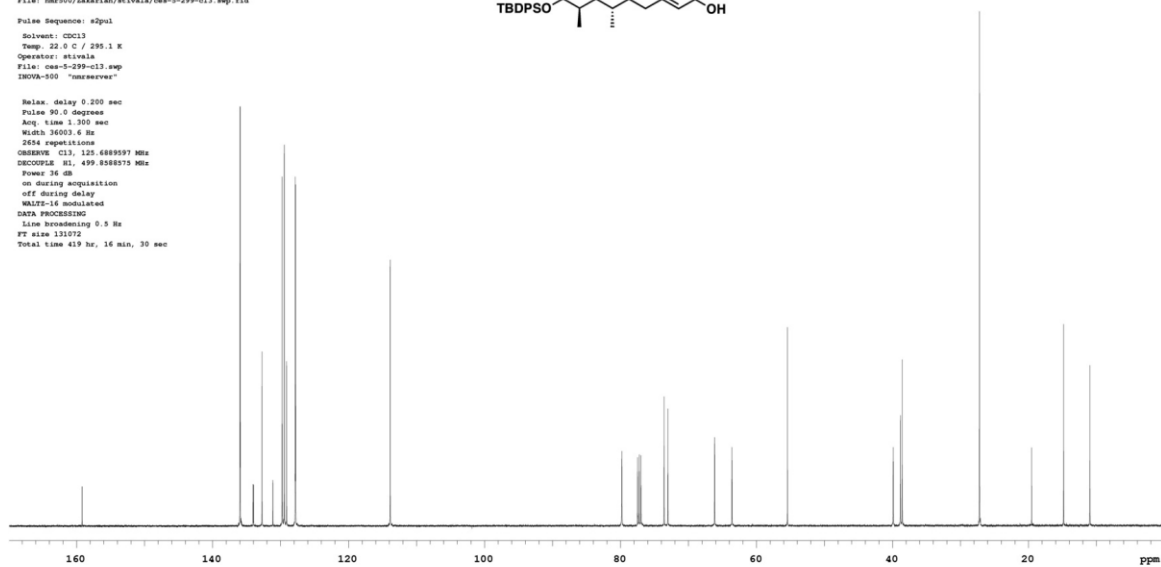
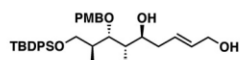
cas-5-290-c13
 File: nmr500/Ekharian/stivaia/cas-5-290-c13.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-5-290-c13.swp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 295 repetitions
 OBSERVE c13, 125.688619 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



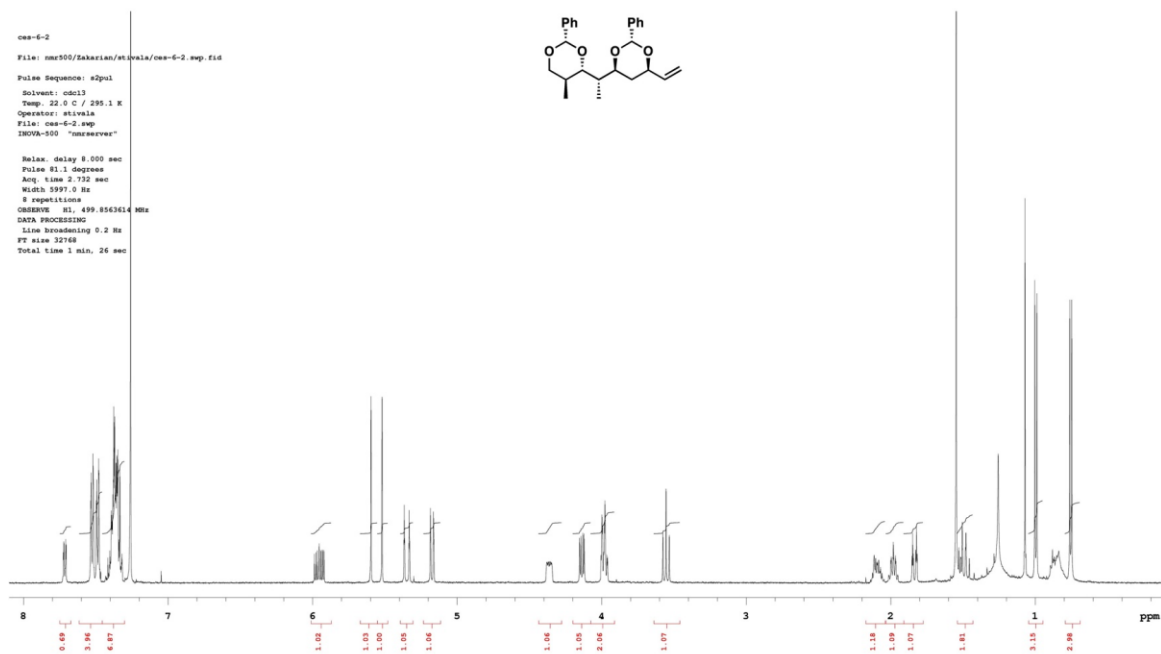
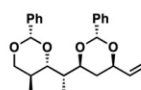
cas-5-295
 File: nmr500/Ekharian/stivaia/cas-5-295.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-5-295.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



cas-5-299-c13
 File: nmr500/Ekharian/stivela/cas-5-299-c13.exp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivela
 File: cas-5-299-c13.exp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 2454 repetitions
 OBSERVE CH1, 125.689597 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



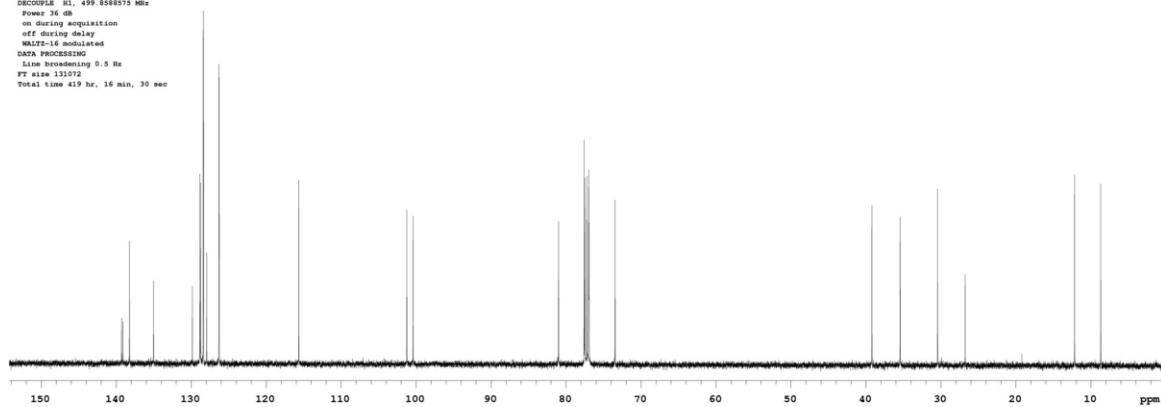
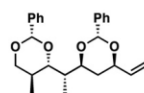
cas-6-2
 File: nmr500/Ekharian/stivela/cas-6-2.exp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivela
 File: cas-6-2.exp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



cas-6-2-c13
File: nmr500/Eakarian/stiva/cas-6-2-c13.exp.fid

Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 22.0 C / 295.1 K
Operator: stiva
File: cas-6-2-c13.exp
INOVA-500 "nmrserver"

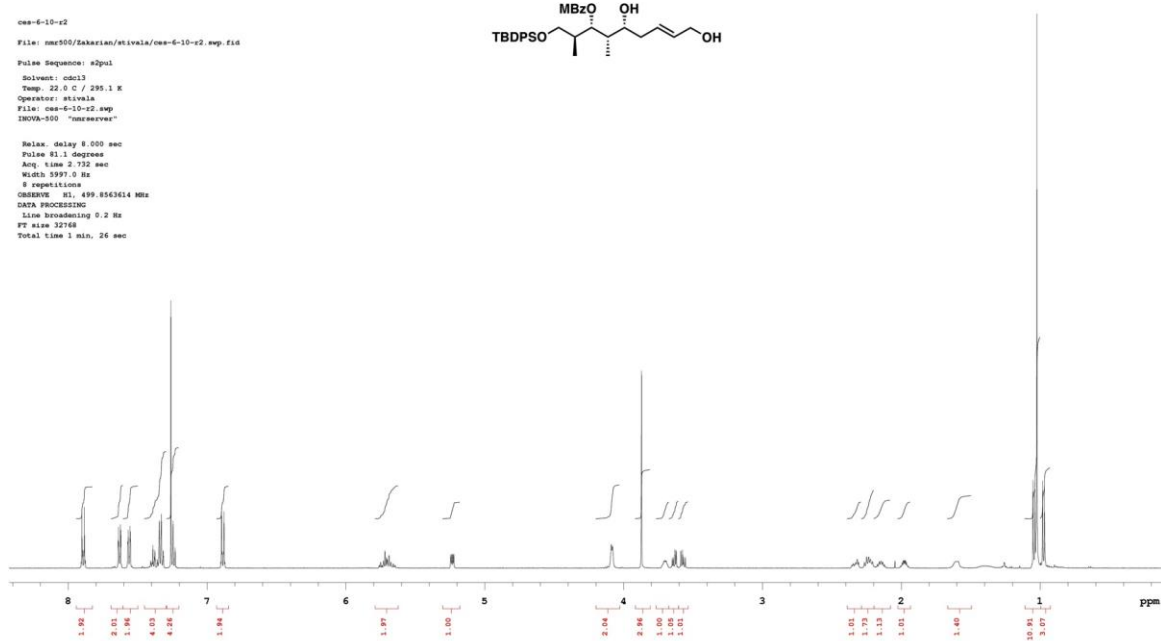
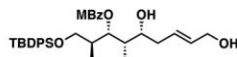
Relax. delay 0.200 sec
Pulse 90.0 degrees
Acq. time 1.300 sec
Width 36003.6 Hz
712 repetitions
GHSBHS c13, 120.689569 MHz
DECOUPLE H1, 499.858875 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 121072
Total time 419 hr, 16 min, 30 sec



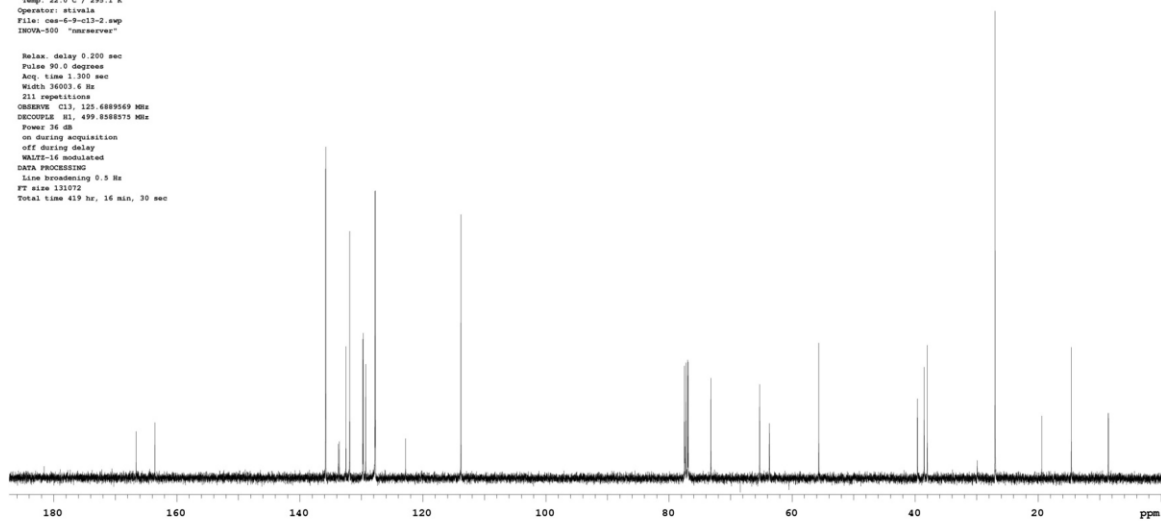
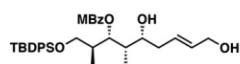
cas-6-10-r2
File: nmr500/Eakarian/stiva/cas-6-10-r2.exp.fid

Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 22.0 C / 295.1 K
Operator: stiva
File: cas-6-10-r2.exp
INOVA-500 "nmrserver"

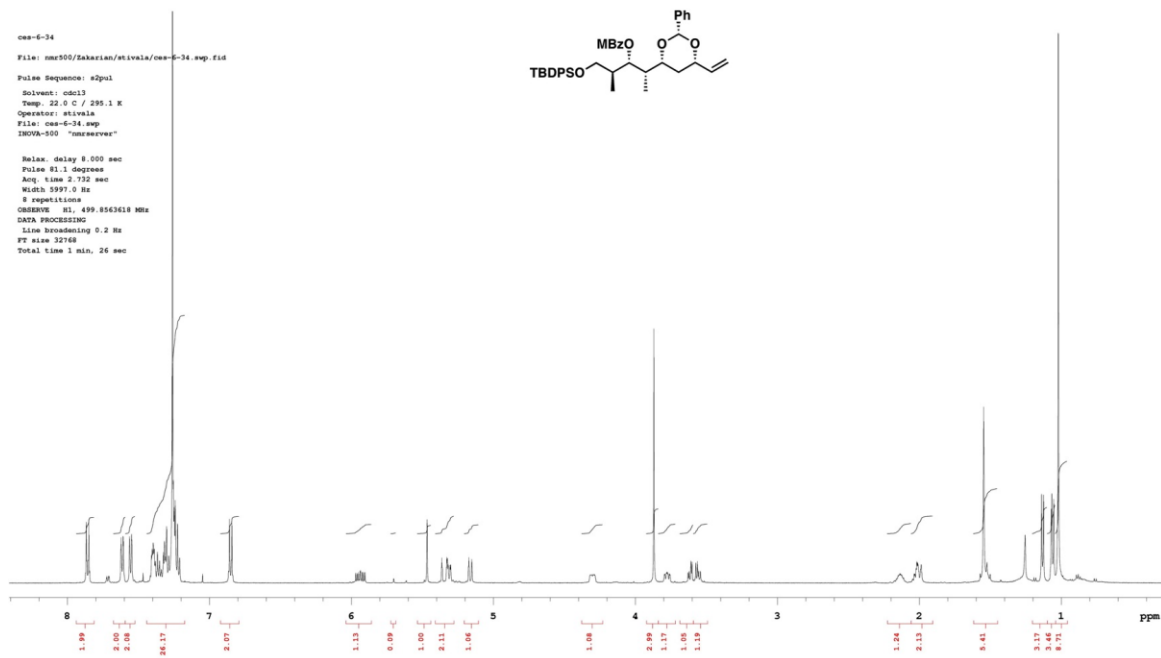
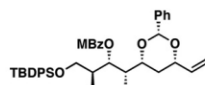
Relax. delay 8.000 sec
Pulse 81.1 degrees
Acq. time 2.732 sec
Width 5997.0 Hz
8 repetitions
GHSBHS H1, 499.856364 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 32768
Total time 1 min, 26 sec



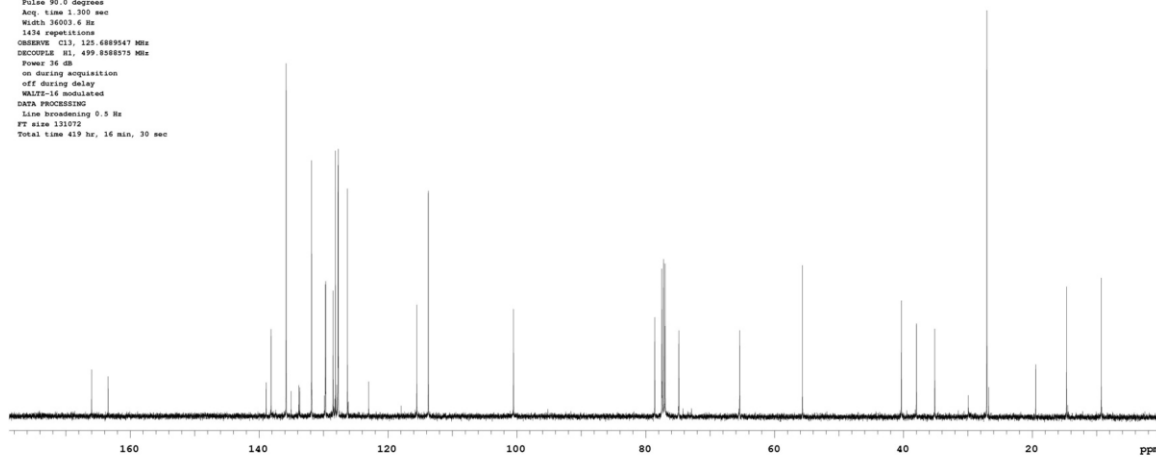
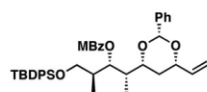
cas-6-9-c13-2
 File: nmr500/Ekharian/stivaia/cas-6-9-c13-2.exp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-6-9-c13-2.exp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 211 repetitions
 OBSERVE c13, 125.689569 MHz
 DECOUPLE H1, 499.858875 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



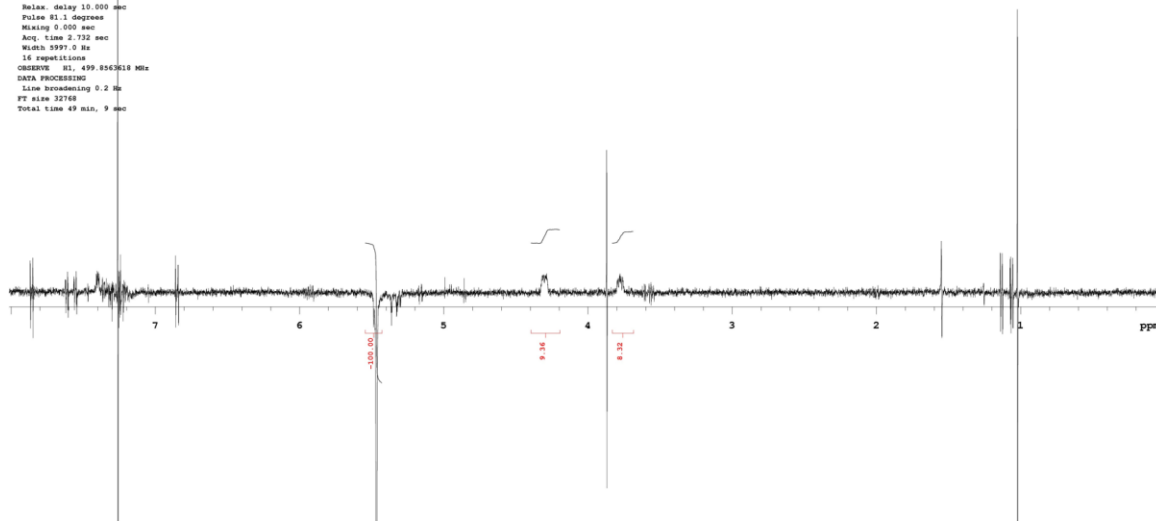
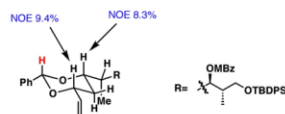
cas-6-34
 File: nmr500/Ekharian/stivaia/cas-6-34.exp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-6-34.exp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

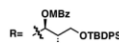
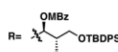


cas-6-34-cl3
 File: nmr500/Ekharian/stivaia/cas-6-34-cl3.exp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-6-34-cl3.exp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 1434 repetitions
 OBSERVE CH1, 125.688547 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec

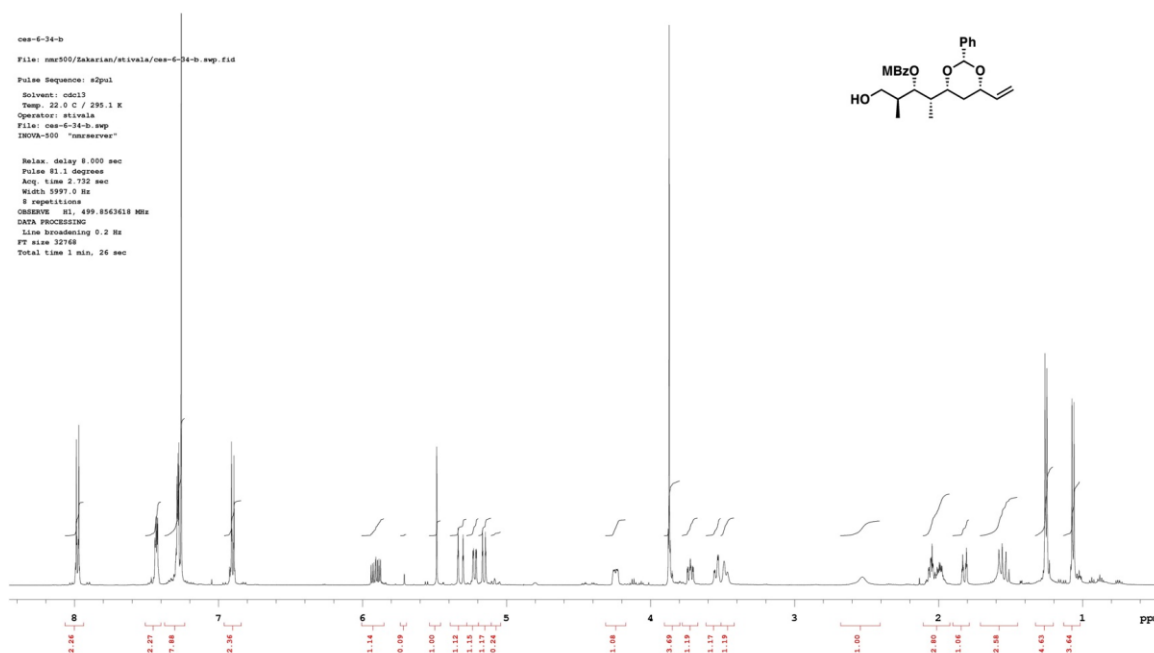
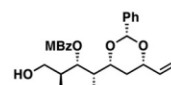


cas-6-34-a-nov
 File: nmr500/Ekharian/stivaia/cas-6-34-a-nov.exp.fid
 Pulse Sequence: cycledm
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cas-6-34-a-nov.exp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse 61.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 49 min, 9 sec

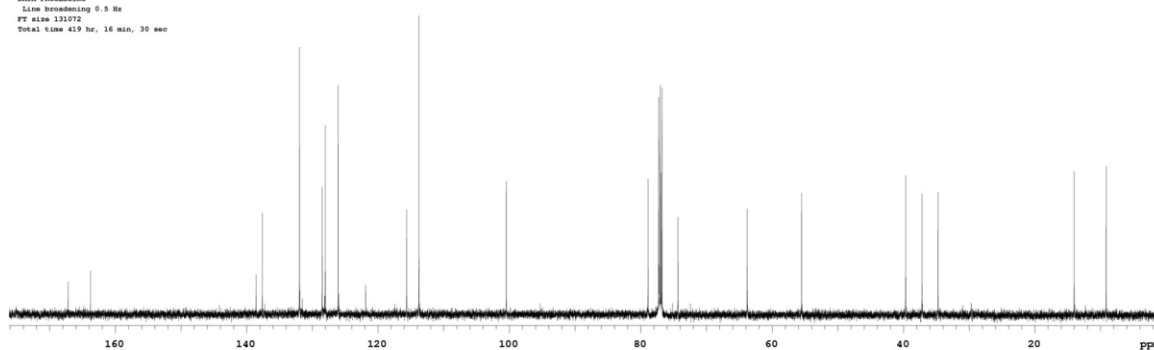
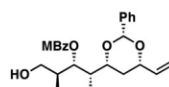




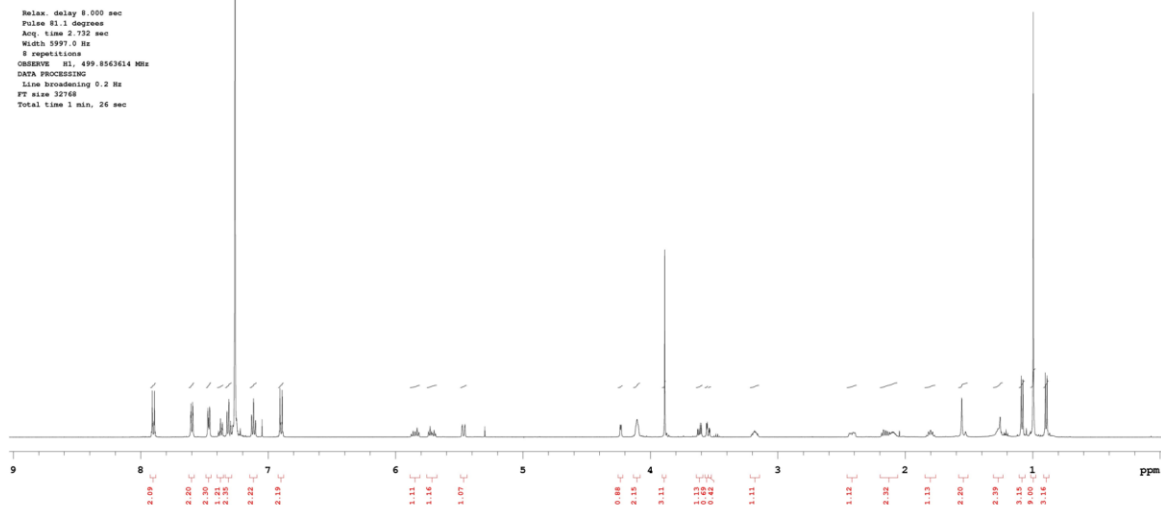
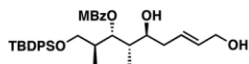
cas-6-34-b
 File: nmr500/Eakarian/stiva/cas-6-34-b.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stiva
 File: cas-6-34-b.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE R1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec



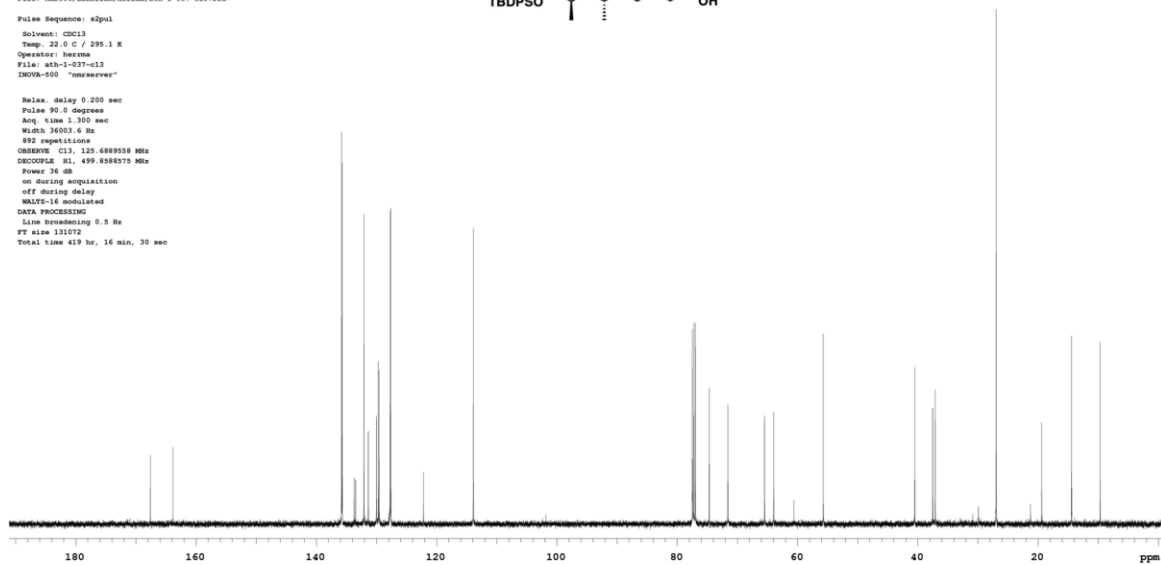
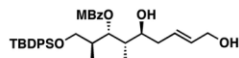
cas-6-34-b-c13
 File: nmr500/Eakarian/stiva/cas-6-34-b-c13.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stiva
 File: cas-6-34-b-c13.swp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 1214 repetitions
 OBSERVE c13, 125.6889813 MHz
 DECOUPLE R1, 499.8588573 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec

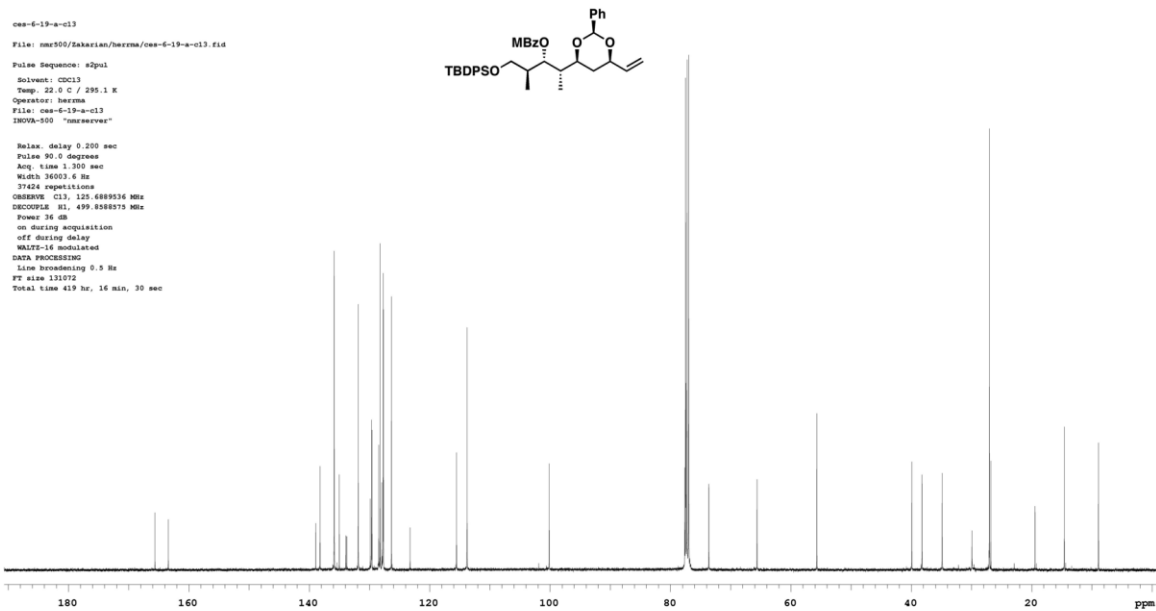
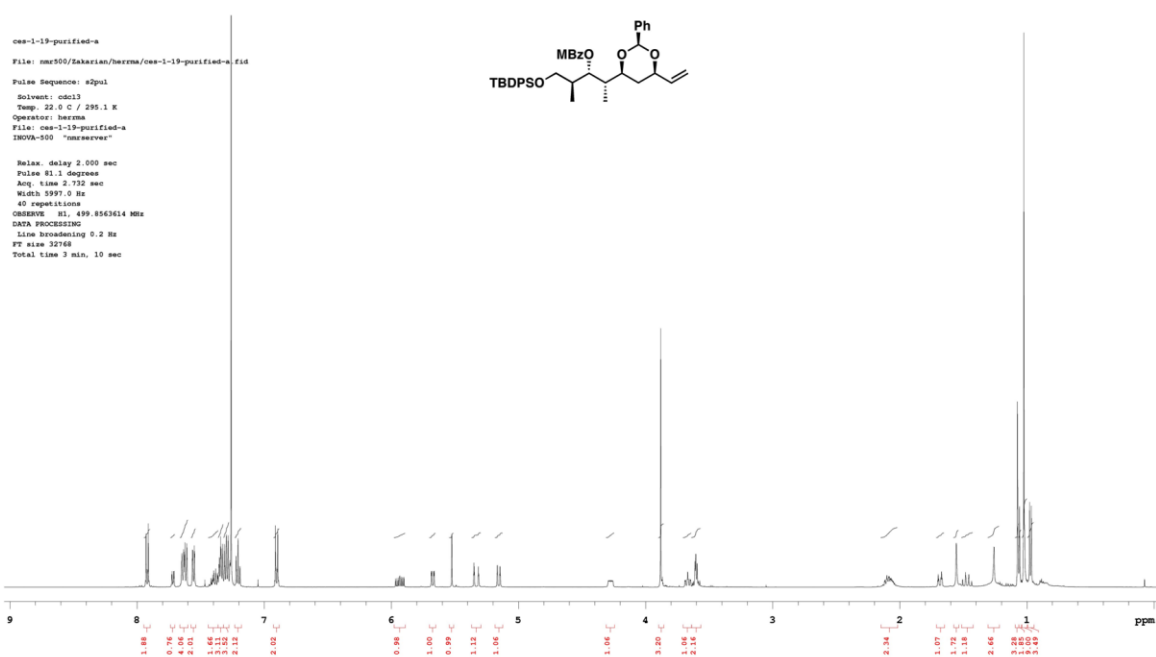


ath-1-037
 File: nmr500/Ekharian/ath-1-037.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: ekharian
 File: ath-1-037.swp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563614 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 1 min, 26 sec

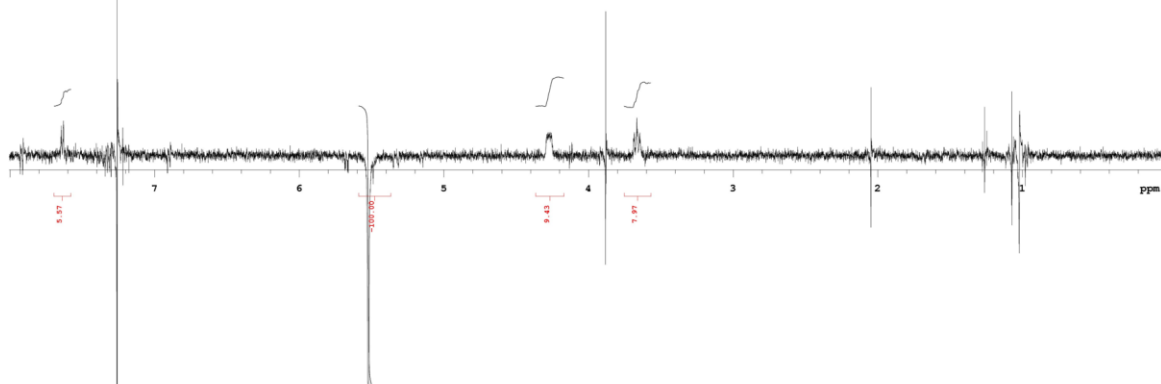
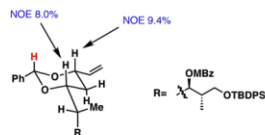


ath-1-037-c13
 File: nmr500/Ekharian/ath-1-037-c13.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: herma
 File: ath-1-037-c13
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.350 sec
 Width 36003.6 Hz
 592 repetitions
 OBSERVE c13, 125.689558 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec

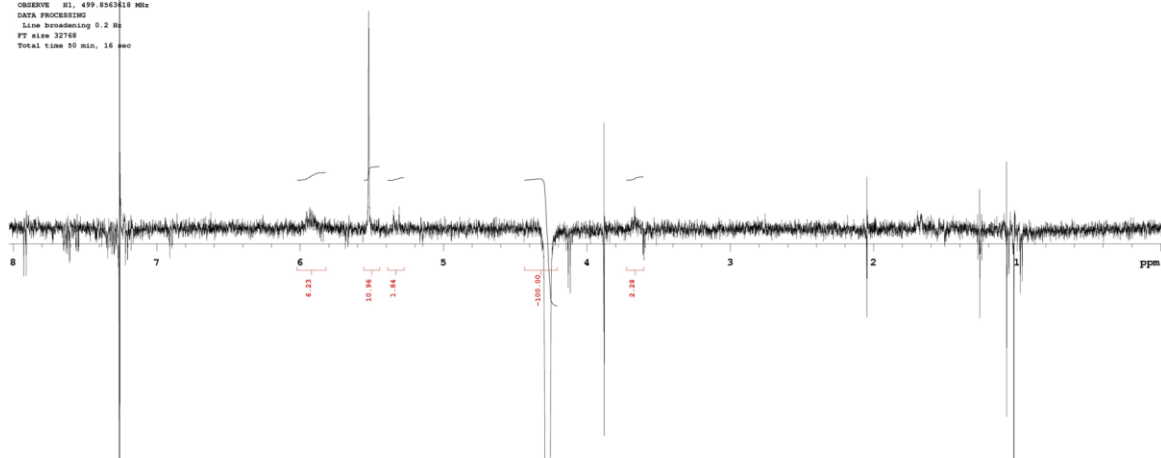
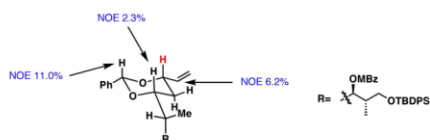




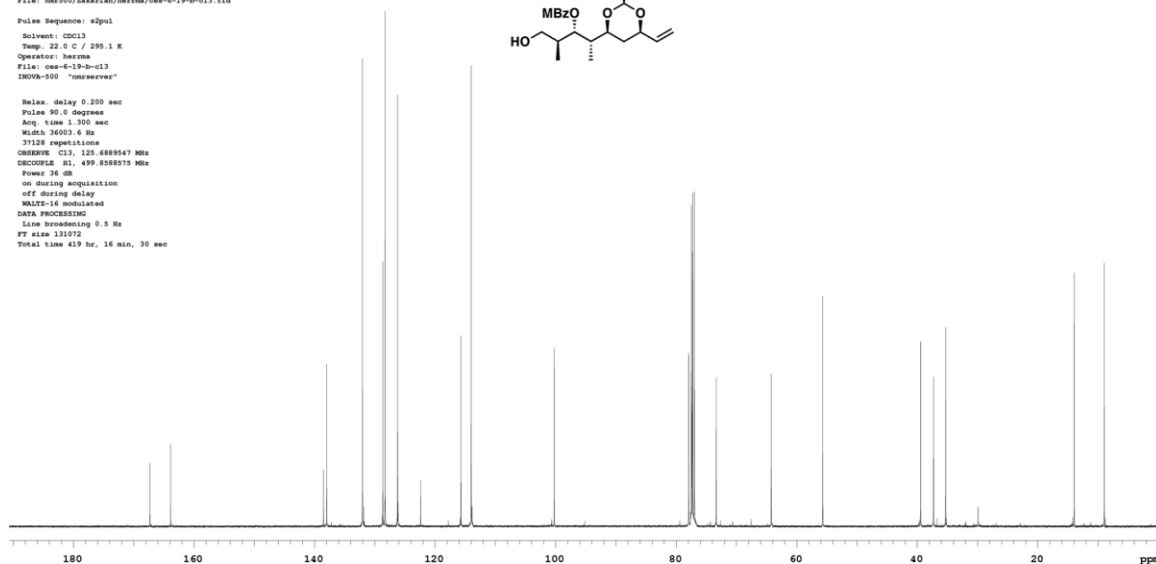
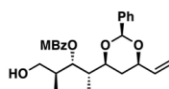
ces-6-19-a-noc
 File: msr505/Ekharian/Alivata/ces-6-19-a-noc.exp.Fid
 Pulse Sequence: cyclanoe
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: Alivata
 File: ces-6-19-a-noc.exp
 INOVA-500 "msrserver"
 Relax. delay 10.000 sec
 Pulse #1.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 12 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 50 min, 16 sec



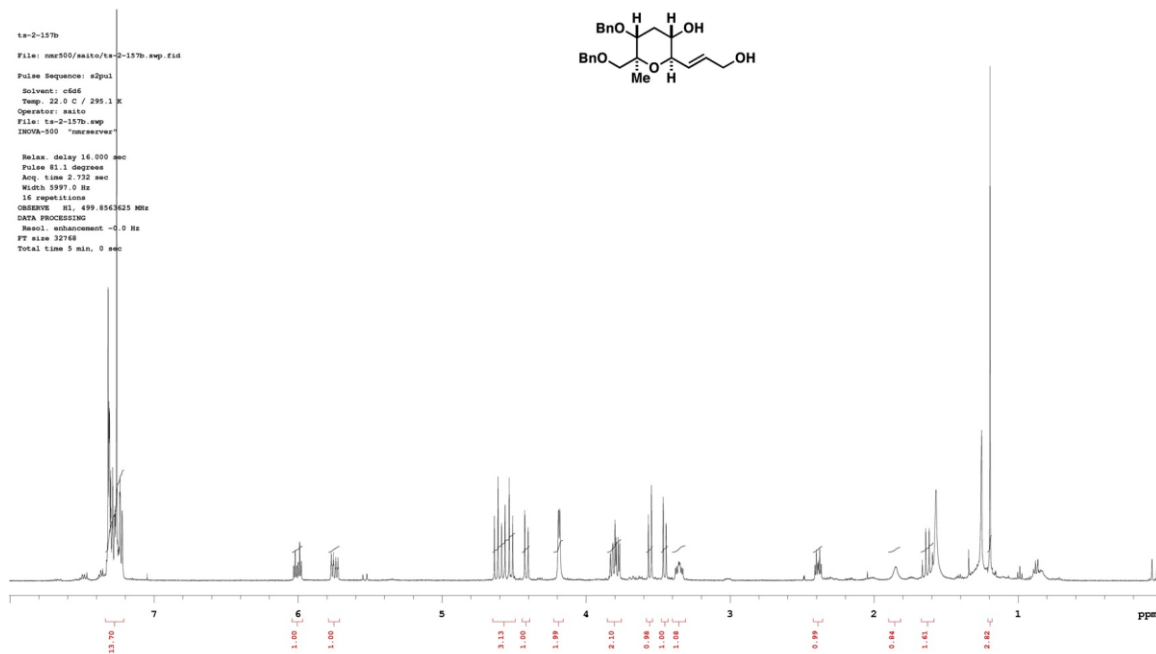
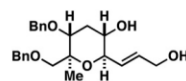
ces-6-19-a-noc
 File: msr505/Ekharian/Alivata/ces-6-19-a-noc.exp.Fid
 Pulse Sequence: cyclanoe
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: Alivata
 File: ces-6-19-a-noc.exp
 INOVA-500 "msrserver"
 Relax. delay 10.000 sec
 Pulse #1.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 12 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 50 min, 16 sec



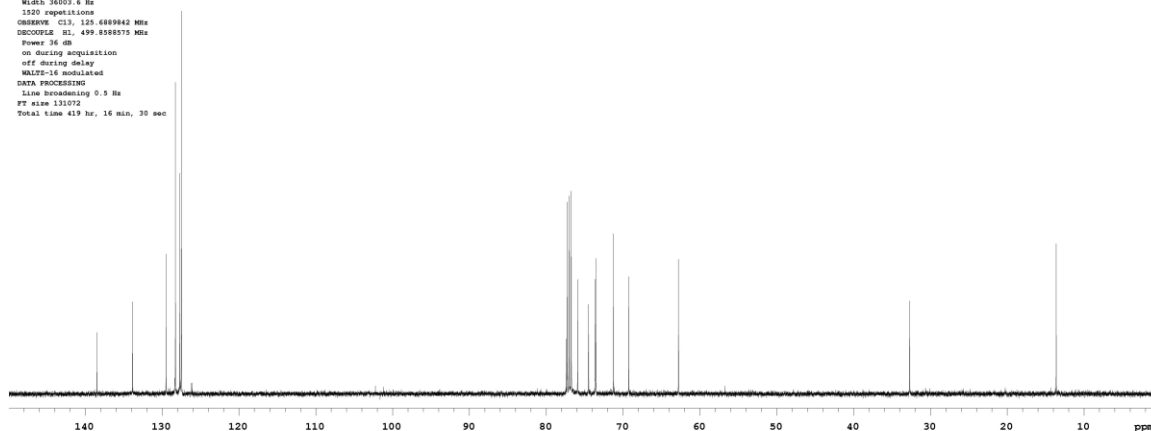
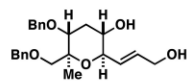
ces-6-19-b-cl3
 File: nmr500/takasima/berma/ces-6-19-b-cl3.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: berma
 File: ces-6-19-b-cl3
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 3603.6 Hz
 37128 repetitions
 OBSERVE c13, 125.689547 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



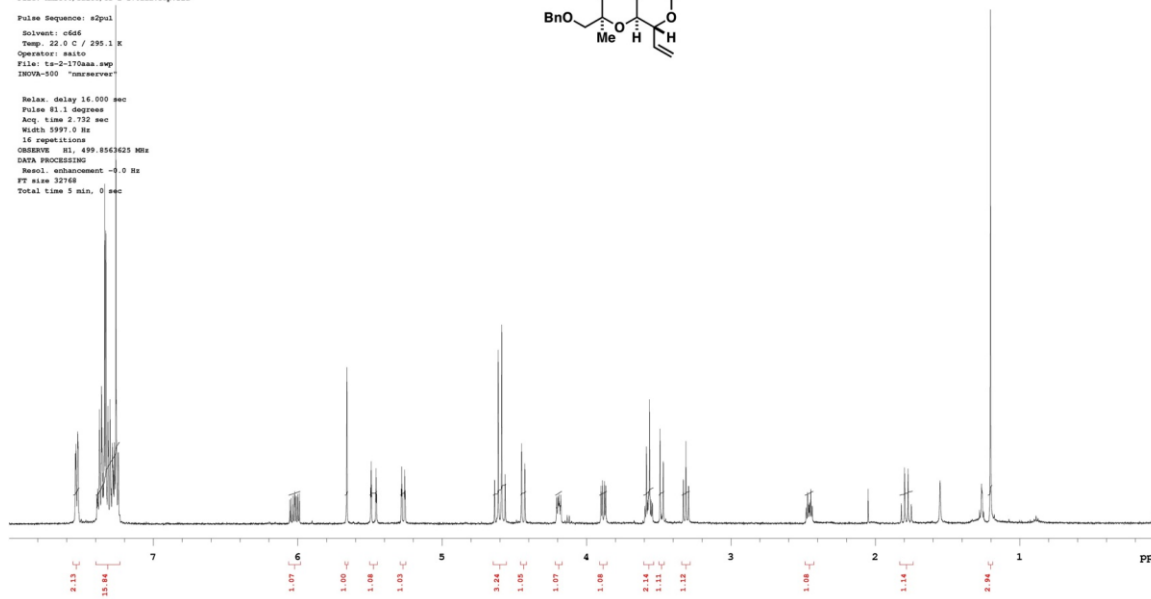
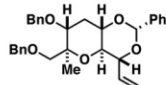
ta-2-157b
 File: nmr500/main/ta-2-157b.exp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: naito
 File: ta-2-157b.exp
 INOVA-500 "nmrserver"
 Relax. delay 16.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.856425 MHz
 DATA PROCESSING
 Recol. enhancement -C 0 Hz
 FT size 32768
 Total time 5 min, 0 sec



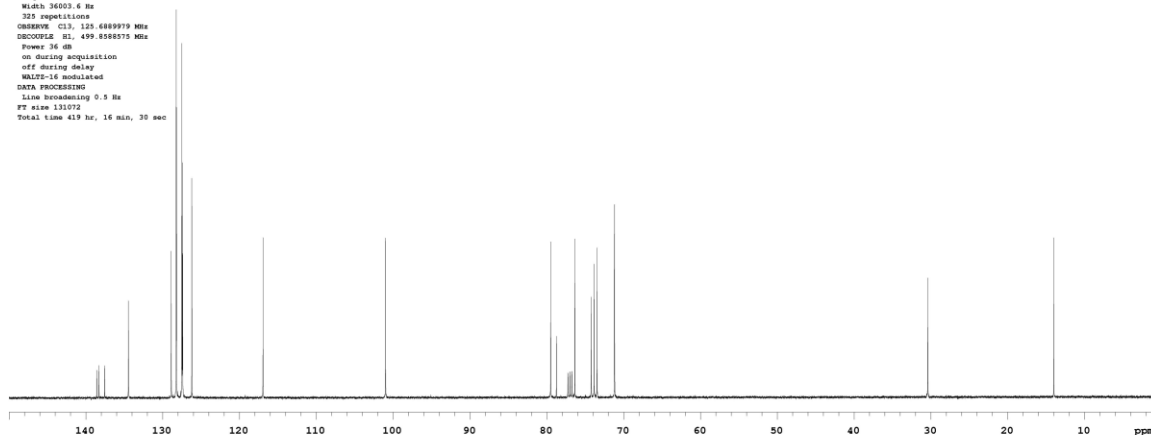
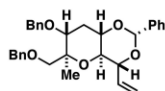
ta-2-157b-13C
 File: mnr500/zakarian/silva/ta-2-157b-13C.exp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: maia
 File: ta-2-157b-13C.exp
 INOVA-500 "masrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.350 sec
 Width 36003.6 Hz
 1520 repetitions
 OBSERVE CH 125.6899842 MHz
 DECOUPLE R1 499.8588575 MHz
 Power 35 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 131072
 Total time 419 hr, 16 min, 30 sec



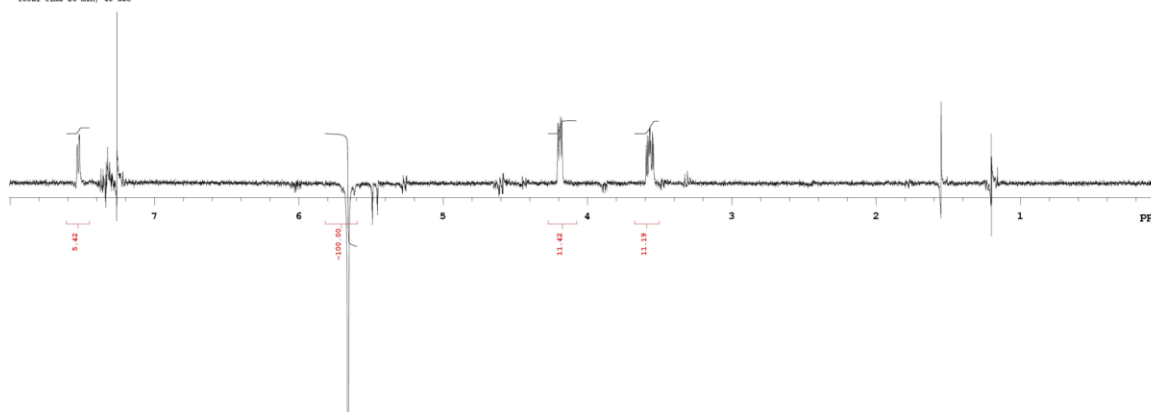
ta-2-170aaa
 File: mnr500/maia/ta-2-170aaa.exp.fid
 Pulse Sequence: s2pul
 Solvent: c6d6
 Temp: 22.0 C / 295.1 K
 Operator: maia
 File: ta-2-170aaa.exp
 INOVA-500 "masrserver"
 Relax. delay 16.000 sec
 Pulse 91.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE R1 499.8563623 MHz
 DATA PROCESSING
 Recal. enhancement -0.0 Hz
 FT size 32768
 Total time 5 min, 0 sec



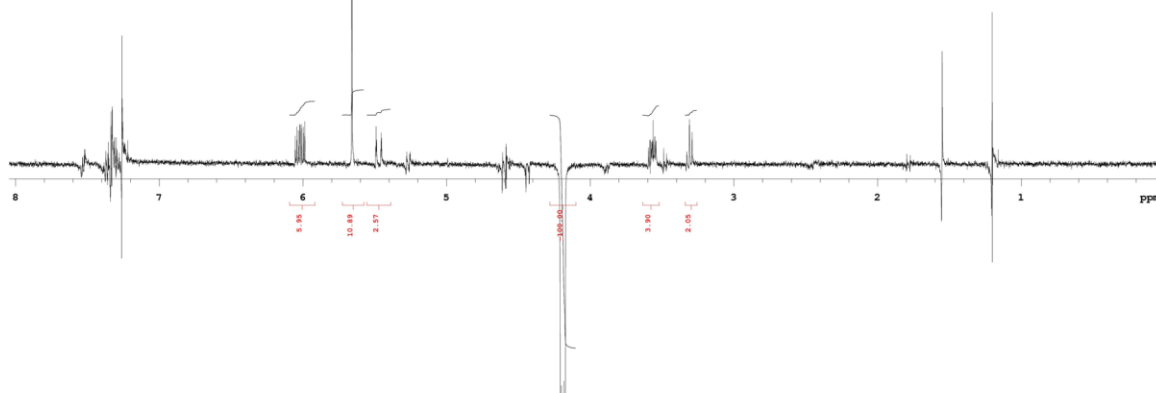
ta-2-170aaa-13C
 File: nmr500/Sakarian/stivaia/ta-2-170aaa-13C.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: ta-2-170aaa-13C.swp
 INOVA-500 "nucserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.350 sec
 Width 36003.6 Hz
 325 repetitions
 OBSERVE CH3 125.688979 MHz
 DECOUPLE R1 499.8588575 MHz
 Power 34 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 131072
 Total time 419 hr, 16 min, 30 sec



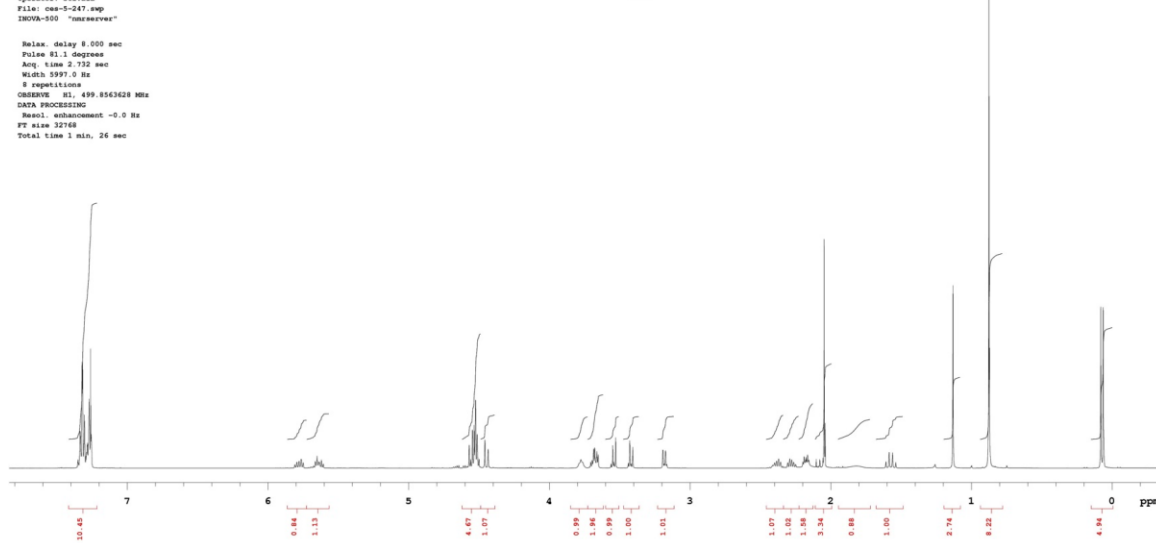
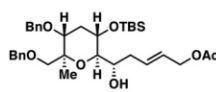
cea-5-239-nuc
 File: nmr500/Sakarian/stivaia/cea-5-239-nuc.swp.fid
 Pulse Sequence: cyclanuc
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: cea-5-239-nuc.swp
 INOVA-500 "nucserver"
 Relax. delay 10.000 sec
 Pulse R1.1 degrees
 Mixing 5.000 sec
 Acq. time 3.732 sec
 Width 5997.5 Hz
 16 repetitions
 OBSERVE R1 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 26 min, 48 sec



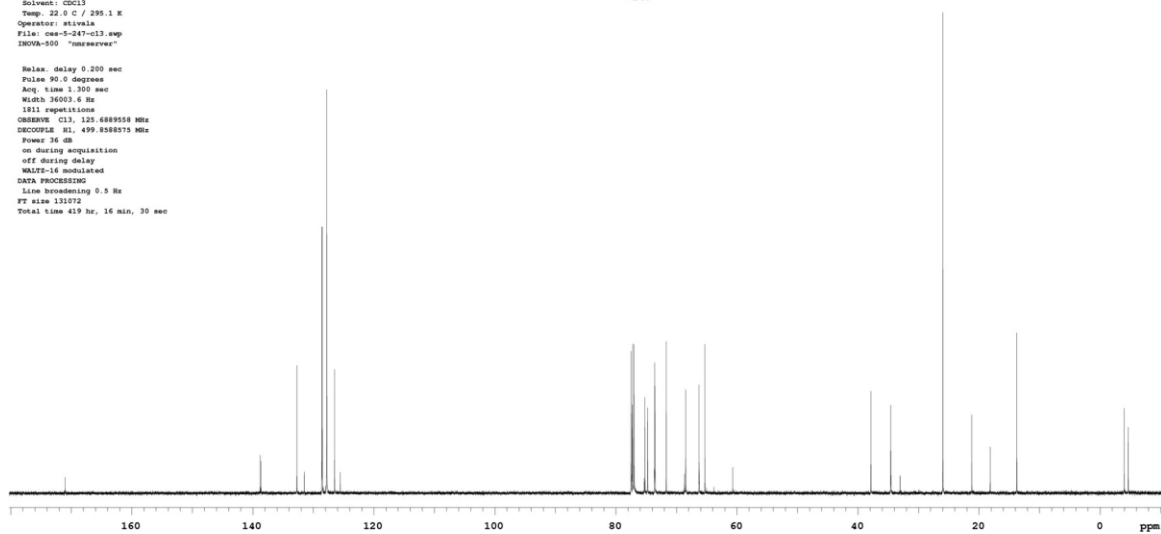
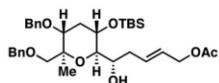
cas-3-239-nme
 File: nmr500/Ekharian/stilva/cas-3-239-nme.exp.fid
 Pulse Sequence: cyclanoe
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stilva
 File: cas-3-239-nme.exp
 INOVA-500 "nmrserver"
 Relax. delay 10.000 sec
 Pulse 61.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Line broadening 0.2 Hz
 FT size 32768
 Total time 26 min, 48 sec



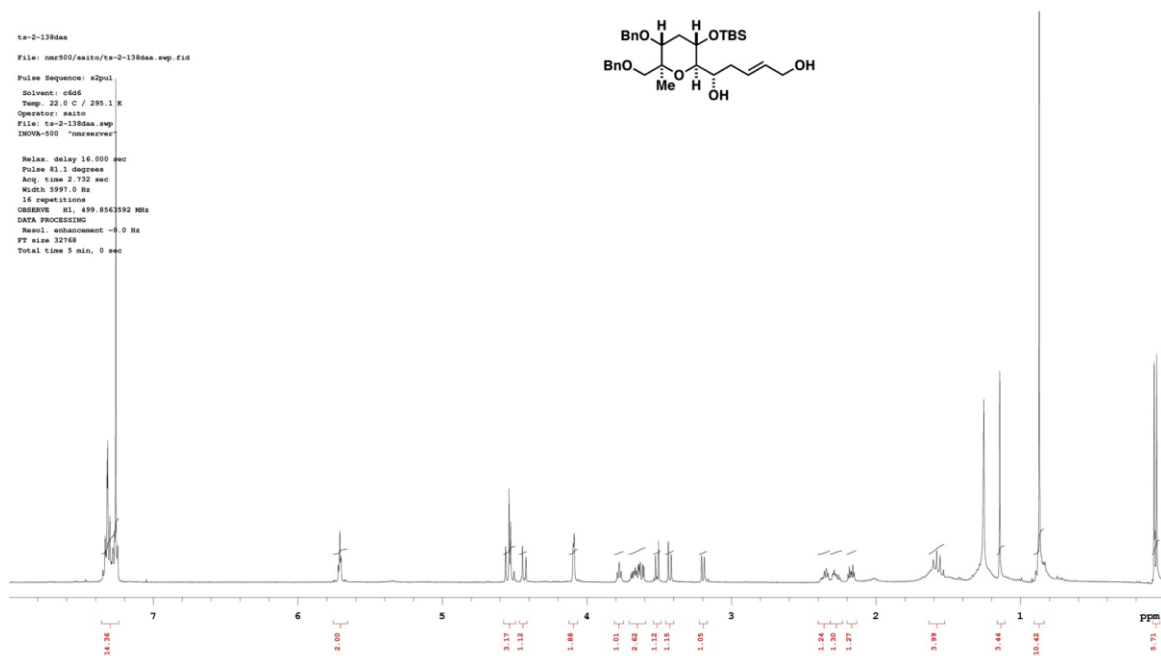
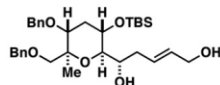
cas-3-247
 File: nmr500/Ekharian/stilva/cas-3-247.exp.fid
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: stilva
 File: cas-3-247.exp
 INOVA-500 "nmrserver"
 Relax. delay 8.000 sec
 Pulse 61.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 8 repetitions
 OBSERVE H1, 499.8563618 MHz
 DATA PROCESSING
 Recol. enhancement -0.0 Hz
 FT size 32768
 Total time 1 min, 26 sec



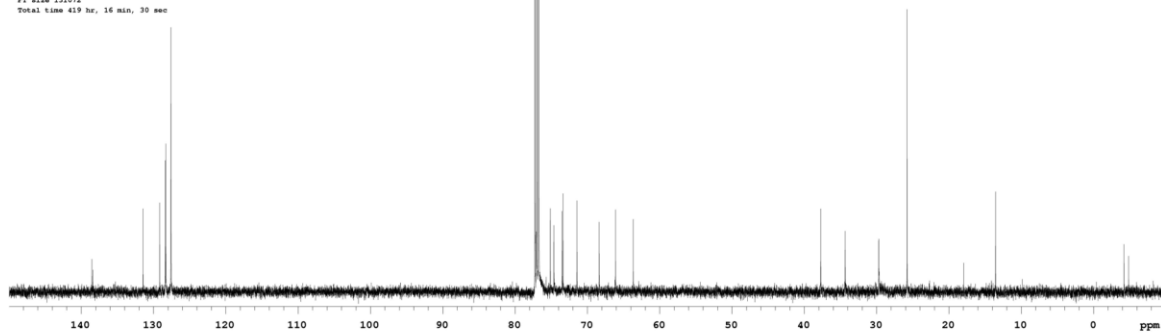
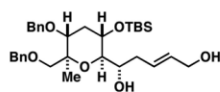
ces-5-247-c13
 File: nmr500/Ekharian/stivaia/ces-5-247-c13.exp.fid
 Pulse Sequence: zgpg30
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: stivaia
 File: ces-5-247-c13.exp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 1811 repetitions
 CQXPM 013, 120.689558 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



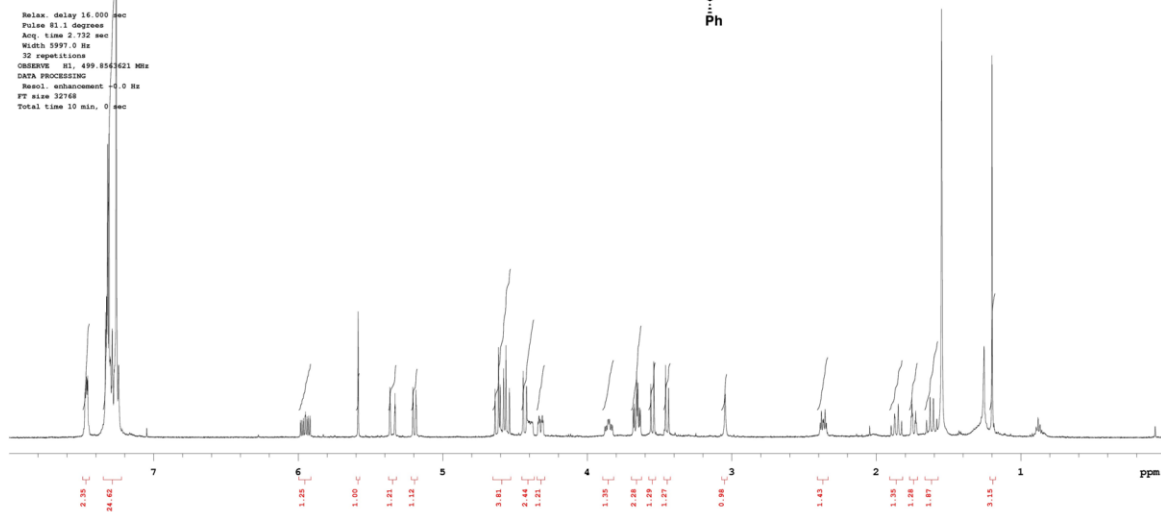
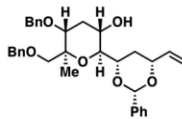
ta-2-138daa
 File: nmr500/saito/ta-2-138daa.exp.fid
 Pulse Sequence: zgpg30
 Solvent: cdcl3
 Temp: 22.0 C / 295.1 K
 Operator: saito
 File: ta-2-138daa.exp
 INOVA-500 "nmrserver"
 Relax. delay 16.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 CQXPM H1, 499.856192 MHz
 DATA PROCESSING
 Recol. enhancement -0.0 Hz
 FT size 32768
 Total time 5 min, 0 sec



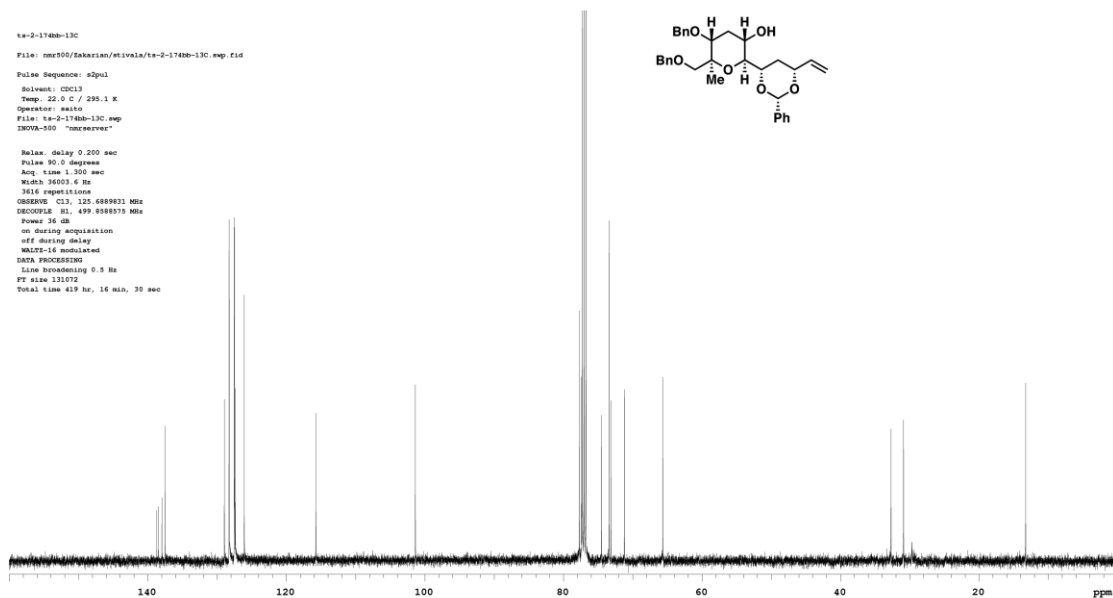
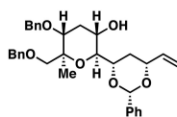
ta-2-138da-13C
 File: nmr500/takasira/stivaia/ta-2-138da-13C.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: naito
 File: ta-2-138da-13C.swp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.200 sec
 Width 36003.6 Hz
 2940 repetitions
 OBSERVE CH1, 125.689814 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



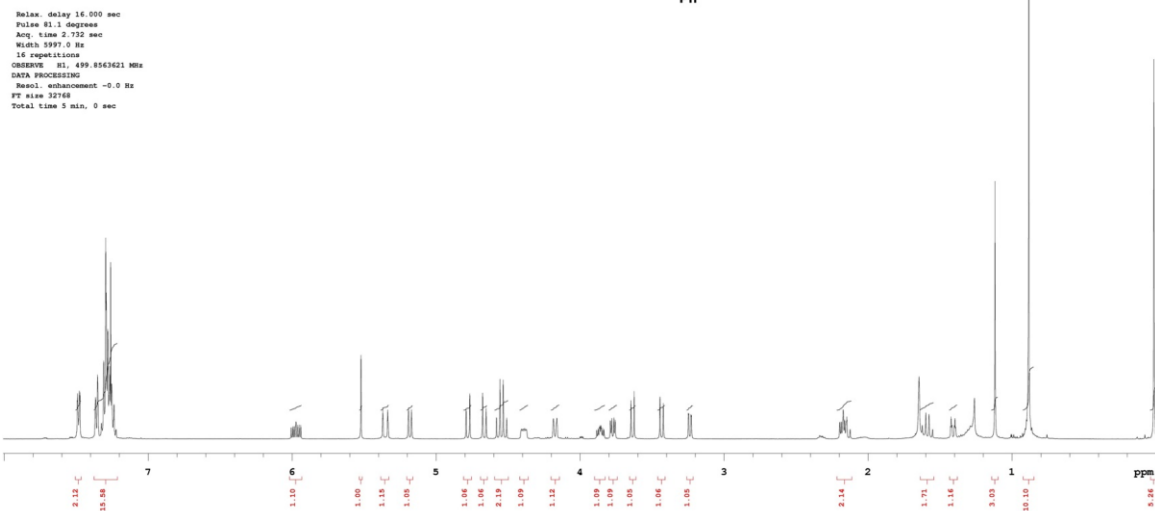
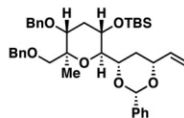
ta-2-141b
 File: nmr500/naito/ta-2-141b.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdd6
 Temp: 22.0 C / 295.1 K
 Operator: naito
 File: ta-2-141b.swp
 INOVA-500 "nmrserver"
 Relax. delay 16.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 32 repetitions
 OBSERVE H1, 499.856421 MHz
 DATA PROCESSING
 Recol. enhancement -0.0 Hz
 FT size 32768
 Total time 10 min, 0 sec



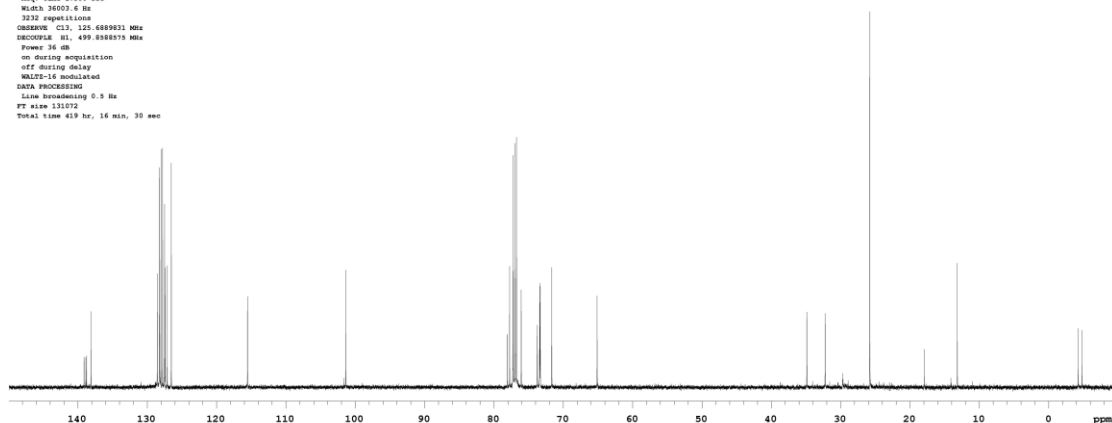
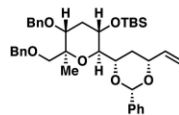
ts-2-174bb-130
File: nmr500/bakerian/mirala/ts-2-174bb-130.exp.fid
Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 22.0 C / 295.1 K
Operator: maino
File: ts-2-174bb-130.exp
INOVN-500 "nmrserver"
Relax: delay 0.200 sec
Pulse 90.0 degree
Acq: time 1.300 sec
Width 36003.4 Hz
3616 repetitions
OBSERVE: CH3, 125.6899611 MHz
DECUPLE: H1, 499.8085573 MHz
Power 36 dB
on during acquisition
off during delay
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 419 hr, 16 min, 30 sec



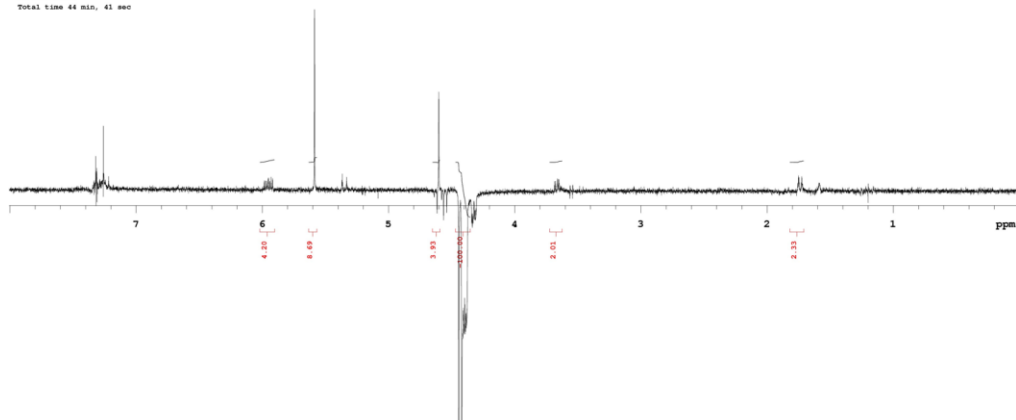
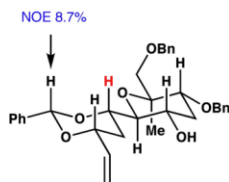
ts-2-171aa
File: nmr500/maino/ts-2-171aa.exp.fid
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 22.0 C / 295.1 K
Operator: maino
File: ts-2-171aa.exp
INOVN-500 "nmrserver"



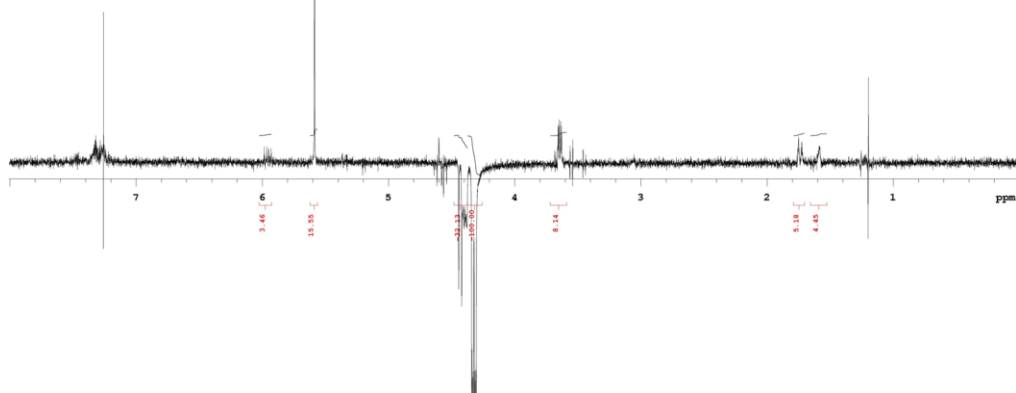
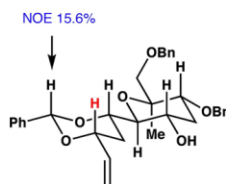
ts-2-171aa-13C
 File: msr500/Sakaria/stivala/ts-2-171aa-13C.exp.fid
 Pulse Sequence: zgpg30
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: maito
 File: ts-2-171aa-13C.exp
 INOVA-500 "mmsurvey"
 Relax. delay 0.200 sec
 Pulse 90.0 degree
 Acq. time 1.300 sec
 Width 36003.6 Hz
 7532 repetitions
 OBSERVE C13, 125.6889631 MHz
 DECOUPLE H1, 499.8585575 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.3 Hz
 FT size 131072
 Total time 413 hr, 16 min, 30 sec



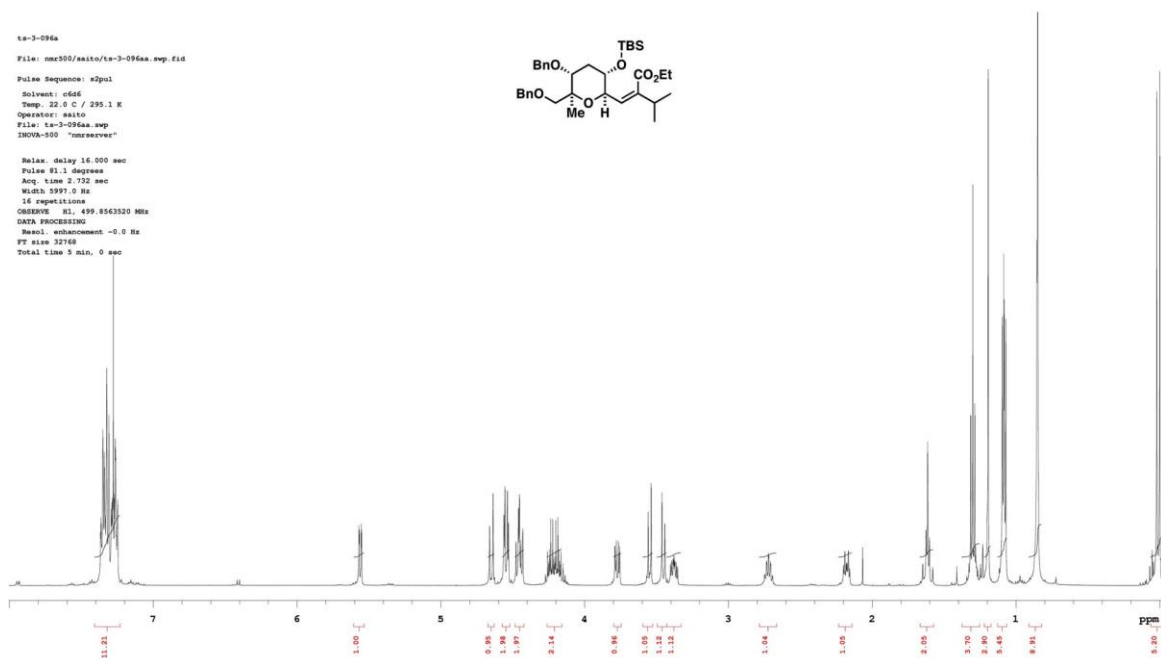
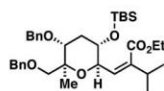
ts-2-1740aa-NOE2
 File: msr500/maito/ts-2-1740aa-NOE.exp.fid
 Pulse Sequence: zgpg30
 Solvent: cddc
 Temp: 22.0 C / 295.1 K
 Operator: maito
 File: ts-2-1740aa-NOE.exp
 INOVA-500 "mmsurvey"
 Relax. delay 10.000 sec
 Pulse 90.0 degree
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563621 MHz
 DATA PROCESSING
 Recal. waltzmodemod -0.0 Hz
 FT size 32768
 Total time 44 min, 41 sec



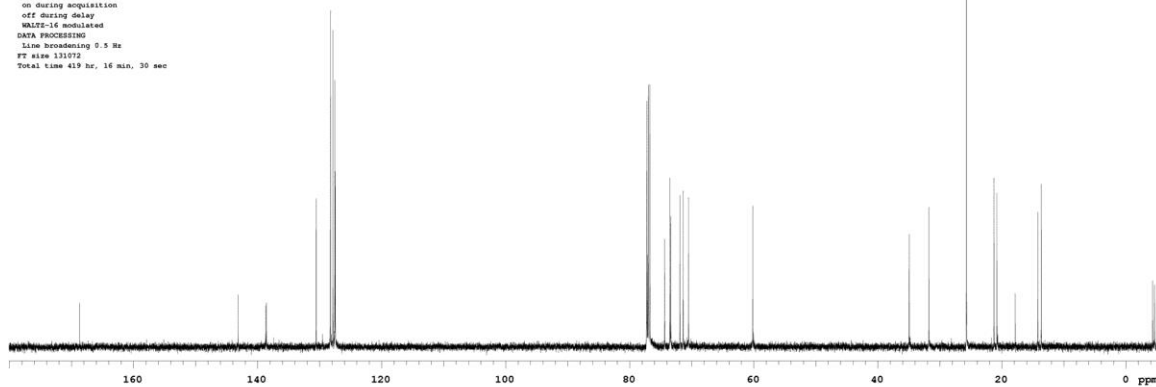
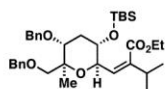
ta-2-174dbb-WOE3
 File: msc305/ta/ta-2-174dbb-WOE.swp.fid
 Pulse Sequence: zgpg30
 Solvent: cdd6
 Temp: 22.0 C / 295.1 K
 Operator: mlto
 File: ta-2-174dbb-WOE.swp
 INOVA-500 "mascerver"
 Relax. delay 10.000 sec
 Pulse 81.1 degrees
 Mixing 0.000 sec
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563621 MHz
 DATA PROCESSING
 Recol. enhancement -0.0 Hz
 FT size 32768
 Total time 44 min, 41 sec



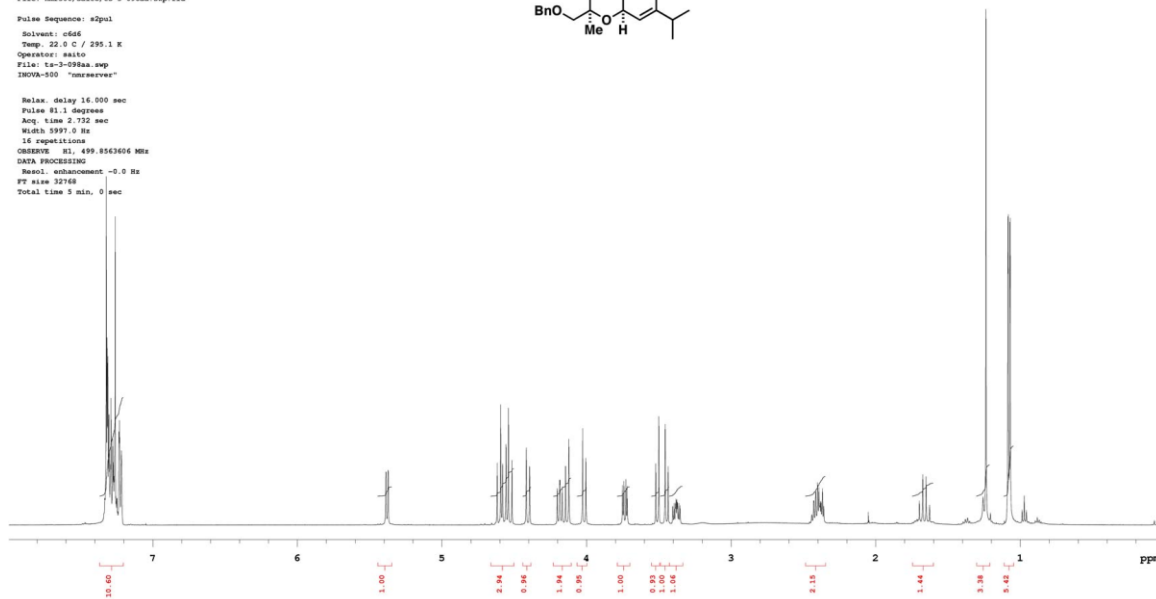
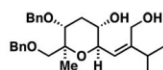
ta-3-096a
 File: msc305/ta/ta-3-096a.swp.fid
 Pulse Sequence: zgpg30
 Solvent: cdd6
 Temp: 22.0 C / 295.1 K
 Operator: mlto
 File: ta-3-096a.swp
 INOVA-500 "mascerver"
 Relax. delay 16.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.8563620 MHz
 DATA PROCESSING
 Recol. enhancement -0.0 Hz
 FT size 32768
 Total time 5 min, 0 sec



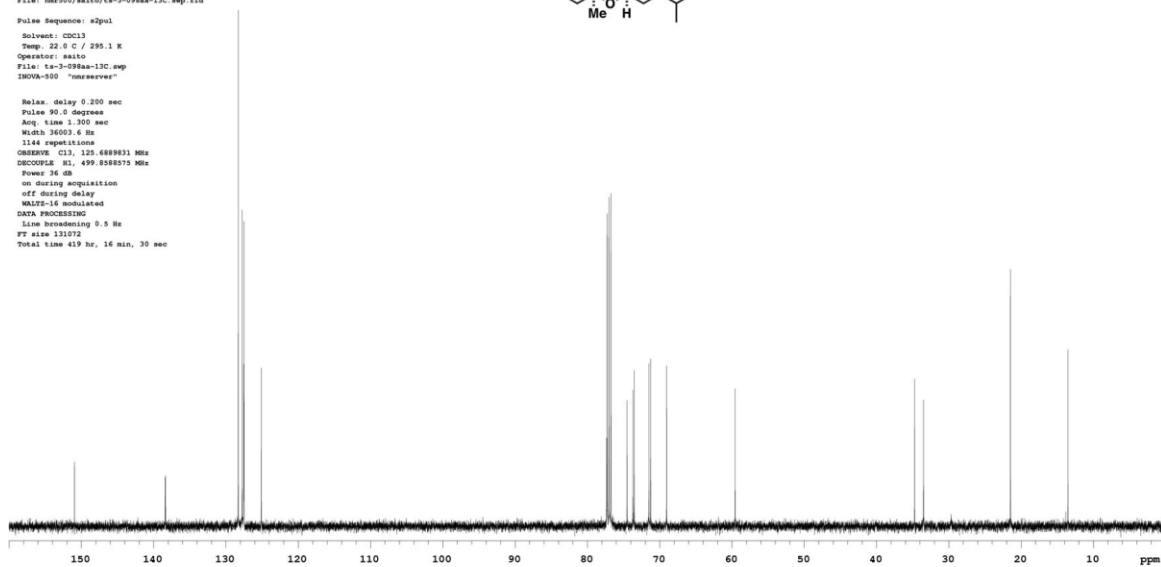
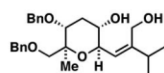
ta-3-096aa-13C
 File: nmr500/maito/ta-3-096aa-13c.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: maito
 File: ta-3-096aa-13c.swp
 INOVA-500 "nmrserver"
 Relax: delay 0.200 sec
 Pules 90.0 degrees
 Acq: time 1.350 sec
 Width 3603.6 Hz
 1712 repetitions
 OBSERVE CH 125.689931 MHz
 DECOUPLE R1 499.858875 MHz
 Power 34 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 131072
 Total time 419 hr, 16 min, 30 sec



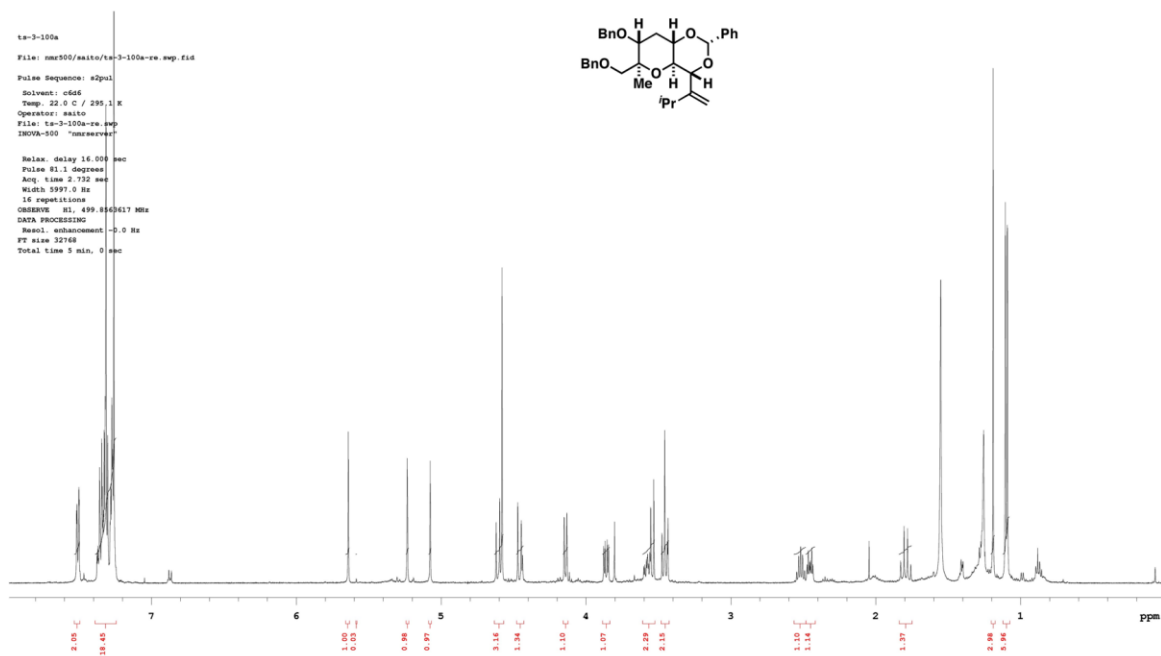
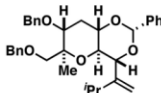
ta-3-098aa
 File: nmr500/maito/ta-3-098aa.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdd
 Temp: 22.0 C / 295.1 K
 Operator: maito
 File: ta-3-098aa.swp
 INOVA-500 "nmrserver"
 Relax: delay 16.000 sec
 Pules 91.1 degrees
 Acq: time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE R1 499.856366 MHz
 DATA PROCESSING
 Recol: enhancement -0.0 Hz
 FT size 32768
 Total time 5 min, 0 sec

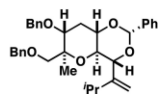


ta-3-098aa-13C
 File: nmr300/mains/ta-3-098aa-13C.swp.fid
 Pulse Sequence: s2pul
 Solvent: CDCl3
 Temp: 22.0 C / 295.1 K
 Operator: naho
 File: ta-3-098aa-13C.swp
 INOVA-500 "nmrserver"
 Relax. delay 0.200 sec
 Pulse 90.0 degrees
 Acq. time 1.300 sec
 Width 36003.6 Hz
 1144 repetitions
 OBSERVE CH1, 125.689831 MHz
 DECOUPLE H1, 499.858873 MHz
 Power 36 dB
 on during acquisition
 off during delay
 WALTZ-16 modulated
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 121072
 Total time 419 hr, 16 min, 30 sec



ta-3-100a
 File: nmr300/mains/ta-3-100a-re.swp.fid
 Pulse Sequence: s2pul
 Solvent: cdd6
 Temp: 22.0 C / 295.1 K
 Operator: naho
 File: ta-3-100a-re.swp
 INOVA-500 "nmrserver"
 Relax. delay 16.000 sec
 Pulse 81.1 degrees
 Acq. time 2.732 sec
 Width 5997.0 Hz
 16 repetitions
 OBSERVE H1, 499.858873 MHz
 DATA PROCESSING
 Recol. enhancement -0.0 Hz
 FT size 32768
 Total time 5 min, 0 sec

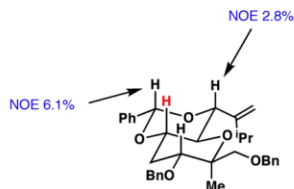




Acq. time 2.732 sec
NUC1 5997.0 Hz
16 repetitions
CDSOURCE RL 499.496321 MHz
DATA PROCESSING
Resol1 enhancement -0.0 Hz
F1 alias 32768
TOTAL time 3 hr, 2 min, 57 sec

6.62
1.02
2.81
3.79
100.00
6.77
1.48

ppm



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Chapter 1

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Chapter 3.5

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Chapter 4

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